NOT CIRCULATE

VOLUME 20 April, 1954 NUMBER 4

UNIVERSITY OF MICHIGAN
APR 13 1954
MEDICAL LIBRARY

THE AMERICAN SURGEON

Editorial Staff

Editor
THOMAS G. ORR, M.D.
Kansas City

Managing Editor
B. T. BEASLEY, M.D.
Atlanta

Associate Editors

MICHAEL E. DEBAKEY, M.D.
Houston

NATHAN A. WOMACK, M.D.
Chapel Hill

J. D. MARTIN, JR., M.D.
Atlanta

CHARLES R. ROUNTREE, M.D.
Oklahoma City

J. DUFFY HANCOCK, M.D.
Louisville

Editorial Board

WILLIAM A. ALTEMEIER, M.D.
Cincinnati

I. A. BIGGER, M.D.
Richmond

BRIAN B. BLADES, M.D.
Washington

LOUIS T. BYARS, M.D.
St. Louis

WARREN COLE, M.D.
Chicago

GEORGE CRILE, JR., M.D.
Cleveland

WARFIELD FIROR, M.D.
Baltimore

KEITH S. GRIMSON, M.D.
Durham

WILLIAM P. LONGMIRE, JR., M.D.
Los Angeles

SAMUEL F. MARSHALL, M.D.
Boston

CHARLES MAYO, M.D.
Rochester

JOHN C. BURCH, M.D.
Nashville

FRANCIS MOORE, M.D.
Boston

ROBERT M. MOORE, M.D.
Galveston

CARL A. MOYER, M.D.
St. Louis

JOHN H. MULHOLLAND, M.D
New York

PHILIP B. PRICE, M.D.
Salt Lake City

R. L. SANDERS, M.D.
Memphis

HARRIS B. SHUMACKER, JR., M.D.
Indianapolis

AMBROSE STORCK, M.D.
New Orleans

HENRY SWAN, M.D.
Denver

GEORGE YEAGER, M.D.
Baltimore

ROBERT M. ZOLLINGER, M.D.
Columbus

PUBLISHED MONTHLY BY
THE WILLIAMS & WILKINS COMPANY
BALTIMORE 2, MARYLAND

COPYRIGHT, 1954, BY THE WILLIAMS & WILKINS COMPANY
Made in the United States of America

Upjohn

one dose
lasts
2 to 4 weeks

Depo-Testosterone

Trademark Reg. U.S. Pat. Off.

CYCLOPENTYLPROPIONATE

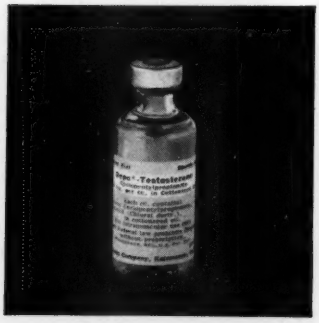
Each cc. contains:

Testosterone Cyclopentylpropionate
.....50 mg. or 100 mg.
Chlorobutanol.....5 mg.
Cottonseed Oil.....q.s.

50 mg. per cc. available in 10 cc. vials

100 mg. per cc. available in 1 cc. and 10 cc. vials

The Upjohn Company, Kalamazoo, Michigan



Entered at the Post Office in Baltimore, Maryland as second-class matter.

CONTENTS, APRIL

Chronic Regional Ileitis: Surgical Treatment and Complications. S. F. MARSHALL, M.D., AND M. P. FECHER, M.D., *Boston, Mass.* 337

Gastric Ulcer and Carcinoma. H. P. PLENK, M.D., AND RU-KAN LIN, M.D., *Salt Lake City, Utah* 348

Management of Pancreatic Cysts and Pancreatic Lithiasis. C. B. PUESTOW, M.D., AND WM. J. GILLESBY, M.D., *Chicago, Ill.* 355

Peritoneal Tap as an Aid in the Diagnosis of Acute Abdominal Disease. WM. H. MORETZ, M.D., AND WM. G. ERICKSON, M.D., *Salt Lake City, Utah* 363

Sarcoma of the Uterus. A Study of Nineteen Patients. P. D. BRUNS, M.D., B. M. PORTER, M.D., AND R. M. MULLIGAN, M.D., *Denver, Colo.* 378

The Use of Femoral Head Prostheses in Fractures. WM. F. STANEK, JR., M.D., J. S. MILES, M.D., L. O. KEYS, M.D., AND H. D. GRAHAM, M.D., *Denver, Colo.* 384

Insulin Induced Stress in the Absence of Epinephrine. G. J. WITTENSTEIN, M.D., *Denver, Colo.* 389

Ischemic Renal Excretion in the Etiology of Experimental Renal Hypertension. J. J. LALLY, M.D., *Kansas City, Mo.* 393

Relief of Postoperative Pain. H. C. DODSON, JR., M.D., AND H. A. BENNETT, M.D., *Oklahoma City, Okla.* 405

Cerebellar Hemangiomas; A Clinico-Pathologic Study of Fourteen Cases. J. M. MEREDITH, M.D., AND G. R. HENNIGAR, M.D., *Richmond, Va.* 410

The Early Diagnosis of Carcinoma of the Esophagus. E. F. PARKER, M.D., *Charleston, S. C.* 424

The Management of Chronic Pancreatitis: A Critical Evaluation. G. B. STARKLOFF, M.D., WM. A. KNIGHT, JR., M.D., AND R. POLLOCK, M.D., *St. Louis, Mo.* 435

Medullary Nailing of Fractures. D. C. HUCHERSON, M.D., *Houston, Texas* 445

Editorials:

Inguinal Hernia in the Older Age Group. R. M. ZOLLINGER, M.D., *Columbus, Ohio* 448

The Surgical Treatment of Direct and Femoral Hernia. H. T. ROBERTSON, M.D., *Denver, Colorado* 449

Book Reviews 334

(In writing to advertisers, please mention the journal—it helps.)

For Intractable Pain

COBROXIN®

(H.W.&D. Brand of Cobra Venom Solution)
50 mouse units per cc.
By Subcutaneous or Intramuscular Injection

'Cobroxin' is a new especially purified preparation of the neurotoxic principle of cobra venom.

'Cobroxin' is being used successfully as a non-habit forming analgesic for the control of intractable pain.[1]

'Cobroxin' is particularly effective in controlling the pain in the terminal stages of cancer.

Detailed information, literature and samples supplied on request.

Supplied in boxes of 25 and 10- 1 cc. ampules.

1. Hills & Firor—Am. Surgeon, Sept. 1952

® Reg. U. S. Pat. Off.

HYNSON, WESTCOTT & DUNNING, INC., Baltimore 1, Md.

THE

AMERICAN SURGEON

Vol. 20, No. 4 April, 1954

CHRONIC REGIONAL ILEITIS: SURGICAL TREATMENT AND COMPLICATIONS

SAMUEL F. MARSHALL, M.D.
MARK P. FECHER, M.D.

Boston, Massachusetts

With increasing experience with the treatment of regional ileitis or cicatrizing enteritis it has become evident that there is a steadily rising incidence of recurrence after all types of treatment, whether medical or surgical. This is evident because the longer the follow-up of these cases, the greater the likelihood for late recurrences. It is now apparent that this disease may recur from 2 years to 8 or even 10 years after operative treatment. Crohn[3] has stated that it is an open question whether any conservative form of medical treatment is warranted in regional ileitis. On the other hand, Kiefer[6] and associates in 1950, in a review of this problem from this clinic, concluded that the medical and surgical methods now in use still are inadequate and far from satisfactory, and that a critical study suggests that medical management is of value in a few cases, and when surgical treatment is employed, additional medical measures postoperatively are necessary and of considerable importance. We are presenting the surgical experience of the Lahey Clinic based upon a study of 223 patients treated surgically for this disease.

Regional ileitis or cicatrizing enteritis is a comparatively infrequent disease, yet it occurs often enough for the physician to be aware of it as a pathologic entity, to become familiar with the difficulty in effectively controlling it and to be informed of its comparatively uncertain prognosis.

Most of the knowledge of this disease has developed since 1932 when Crohn, Ginzburg and Oppenheimer[4] reported a series of 13 cases in which the terminal ileum was involved, and used the term regional ileitis to describe this pathologic

From the Department of Surgery, Lahey Clinic, Boston, Massachusetts.
Read before the Southwestern Surgical Congress, Salt Lake City, Utah, September 23, 1953.

TABLE I

Regional ileitis, age and sex

(Operations on 223 Patients)

Age Incidence

Years	Cases	Per cent
11–20	33	14.8
21–30	57	25.6
31–40	73	32.7
41–50	36	16.1
51–60	16	7.2
61–70	8	3.6
Total	223	

Sex Incidence

Males	112
Females	111
Total	223

entity. Since this report voluminous literature has arisen regarding this disease. In an article on its pathology in 1948,[8] attention was directed to a review of 206 articles on this subject. Kiefer reported that regional ileitis had occurred 70 times in 100,000 admissions at the Lahey Clinic.

All races are represented and reported in the literature and the disease affects patients of any class or social position; it also affects every age, although there is a paucity of cases in the very young and the very old. The ratio of age groups is similar to those given in other series in the literature. In our series of 223 patients operated upon, 73 per cent were between the ages of 11 and 40 years (table I). Bockus[1] stated that 75 per cent are between the ages of 20 and 40 years.

PATHOLOGY

Much has been written regarding the pathologic features of this disease and the reader is referred to the literature for this description. An excellent presentation is given by Warren and Sommers.[8, 9]

Of greater significance to the surgeon and the internist is the ability to distinguish regional ileitis from ulcerative colitis. It is common to see patients in whom, after surgical treatment, the disease recurs with widespread and fulminating involvement of the colon which may require ileostomy and total colectomy for eventual control of the disease. In this group of 223 patients treated surgically, we have noted seven instances of recurrence associated with extensive colon involvement that required ileostomy and total colectomy. Such wide involvement of the colon must not be confused with cases of regional ileitis involving the terminal ileum, in which the disease process often extends into the cecum and colon, at least in the initial phase of the disease, but it is rarely widespread in the

colon. Warren and Sommers,[9] in a study of the pathology of regional ileitis and its relation to the pathology of ulcerative colitis (much of whose material comes from operative specimens of the Lahey Clinic), stated that in 15 per cent of 300 pathologic specimens the disease process extended to the colon.

Warren and Sommers also stated that ulcerative colitis involved the terminal ileum in 34 per cent of the cases, producing ulcerative ileocolitis, and that since the affected portions of the bowel may overlap, it is not possible to consider that colonic involvement excludes regional ileitis or that involvement of the ileum definitely rules out ulcerative colitis. It is their belief from this pathologic study of these specimens that the morphology of the two disease processes is as different as syphilis is from gonorrhea and that these two pathologic conditions are microscopically distinguishable and rarely coexist. Their study of the pathology in regional enteritis showed progressive sclerosing granulomatous lymphangitis and an edematous elephantiasic cicatrization of the entire intestinal wall with involvement of the mesenteric regional lymph nodes. In regional ileitis, with the exception of the involvement of the intestine and mesenteric lymph nodes, there appeared to be no related pathologic lesion save for the occasional similar granulomas in the liver. It is their conclusion that ulcerative colitis is recognized as an exudative inflammatory process, restricted to the colon and to the mucosa and submucosa. On the other hand, the evidence of involvement of other body organs suggests that ulcerative colitis may be a disease process of the entire body.

Regional enteritis is characterized as a chronic pathologic process which is progressive and which lasts over the course of many years. The onset of the disease may be an acute process, the usual course is chronic and intermittent and, as stated above, the inflammatory changes involve all layers of the small intestine with extensions into the mesentery and the lymph nodes. The disease is attended by scarring, the development of a mass usually involving the terminal ileum, formation of fistulas of ileal origin and the occurrence of rectal complications. The clinical course is indicated by abdominal pain, low grade fever, mild diarrhea, secondary anemia and a progressive loss of weight plus the systemic effects of long-standing, chronic infection.

DIAGNOSIS

The diagnosis of regional enteritis is established by roentgenologic studies which in most cases are quite characteristic. Kiefer has pointed out that roentgen examination of the bowel shows obliteration of the mucosal pattern, coarsening and polypoid changes, and rigidity and narrowing of the small intestine. There also may be dilatation of the bowel above the area of narrowing and rigidity which may produce obstruction. Frequently a tender, fixed mass is present in the right lower abdominal quadrant, and the diagnosis is strongly suggested by the presence of such a fixed mass and the evidence of long-standing, chronic infection.

The history of previous abdominal operations with no improvement in the patient's condition is of some importance. In this group of 223 patients, only 109 patients had had no previous abdominal operation before admission to the clinic, whereas in the remainder of this series 114 patients had had a total of 209 opera-

TABLE II

*Operations Prior to Admission**

(223 Patients)

Appendectomy	73
Resection of small bowel	18
Ileocolostomy	18
Resection of ileum and ascending colon	19
Exploration	19
Closure of fistula (attempted)	14
Relief of intestinal obstruction	12
Drainage of abdominal abscess	11
Operation for rectal fistula	13
Ileostomy	4
Colostomy	4
Drainage of rectal abscess	3
Entero-enterostomy	1
Total	209

* No operation, 109 cases.

tive procedures, which are indicated in table II. One of the most common abdominal operative procedures was appendectomy, which was done in 73 patients. In 16 of the patients who had appendectomy, fistulous tracts later developed, leading from the ileum to the abdominal wall. Most of this group had had numerous surgical attempts to close the fistula without apparent recognition of the underlying disease.

The numerous operations done in this group are indicative of the fact that the clinical picture of this disease was not recognized and frequently the pathologic entity was not diagnosed correctly at the time of laparotomy and some abdominal procedure was done other than a definite surgical procedure for this condition.

One of the characteristic clinical features is the formation of fistulas. These fistulas lead from the ileum to the abdominal wall and frequently from the ileum to loops of the small bowel, to the sigmoid or to other adjacent viscera. We have had several instances of bladder fistulas, and with the development of pelvic abscesses it is not unusual to see perineal or pelvic fistulas.

Rectal complications of a suppurative nature are also characteristic manifestations of this disease. In this series 13 patients had had operations for rectal fistulas and 3 had had drainage of rectal abscesses. These fistulas develop as a result of perforation of the diseased bowel with penetration of the adjacent viscera. If perforation occurs without development of a fistula, it is common for intra-abdominal abscesses to develop. In this series of 223 patients, 11 had had drainage of abdominal abscesses before they were admitted to the clinic.

It is well recognized that spontaneous remissions of this disease are infrequent, yet may occur, but surgical treatment is indicated in the larger percentage of cases of regional ileitis. Since the pathologic entity is progressive and the disease usually lasts over a period of many months or years, intestinal obstruction usually develops and is a common complication for which a surgical procedure

must be undertaken. As stated above, only 109 patients in the series of 223 had had no previous abdominal operation before admission; 114 patients had a total of 209 operative procedures, many of them multiple procedures, and some had had as many as eight operations before the true nature of the pathologic process was recognized. In 14 patients an attempt was made to close abdominal fistulas which had occurred following appendectomy. In only 37 patients was a resection of the small bowel or of the ileum and ascending colon done on the basis of a diagnosis of regional ileitis.

TREATMENT

The treatment of this condition presents a difficult problem because of the high recurrence rate following both medical and surgical measures. The etiology of regional enteritis is unknown and the disease process commonly affects the terminal ileum of a young adult of either sex or any race, but the jejunum, upper ileum, cecum or colon may also be involved. Kiefer and co-workers, in a previous discussion of this problem from this clinic, stated that in general there are three methods of treatment and, on the whole, none is completely satisfactory. These methods are: (1) medical, (2) conservative surgical procedures—such as drainage of an abscess or sidetracking operations without removal of the disease process—and (3) radical surgical extirpation of the diseased bowel.

In general, the indications for medical treatment are (1) localized disease of short duration without complications such as fistulas, abscesses or obstruction, and (2) widespread disease which may involve so many segments of the small intestine that removal of the diseased intestine would seriously interfere with digestive absorption.

Our preference at the Lahey Clinic has been for the utilization of primary resection in the majority of cases. In the earlier years resection was done by the two stage Mikulicz procedure. More recently we have resected the diseased bowel—in most cases the terminal ileum with removal of the cecum and ascending colon—followed by primary anastomosis of the small bowel to the transverse colon. The cecum and colon were resected because of the frequent extension of the disease to the colon.

We have not adopted the operative procedure of ileotransverse colostomy, a sidetracking operation advocated by the Mt. Sinai group of Crohn,[3, 4] Garlock[5] and associates, because it is our opinion that the removal of all diseased loops of bowel offers a better prospect of control of the disease. Resection of any ulcerated, infected segment of intestine removes a focus of the inflammatory process with any fistula that may be present, and offers much better control of the infection. It also prevents development of the complications which can occur when an infected segment of the intestine is retained.

In the group of 223 patients admitted to the clinic, 18 had previously had ileocolostomy to divert the intestinal contents past the diseased bowel, and all 18 subsequently came to resection because of continued distress with increasing difficulty. As pointed out by Warren and Sommers, with the diseased loop of bowel retained in the abdomen the disease tends to extend upward along the

TABLE III

Ileocolostomy—18 cases; duration before admission to Lahey Clinic

	Cases
Less than 1 year	3
1 year or more	3
2 years or more	2
3 years or more	2
4 years or more	4
Over 5 years	4
Total	18

All patients had resections after admission.

intestine, and in most of these cases which we have resected in which an ileocolostomy had been done previously elsewhere, the ileocolostomy stoma was involved with the granulomatous lesion and there was consequent development of obstruction. Persistent active intraluminal inflammation and ulceration was observed in all of these patients and frequently the sidetracked loop was found to be obstructed and markedly ulcerated, and acted as a definite focus for serious intra-abdominal suppuration.

We rarely have used ileocolostomy without resection except in the presence of abdominal abscess or when the patient's condition did not permit a radical resection of the bowel without vastly increased risk. In all of these cases after drainage of the abscess and improvement in the patient's condition we later planned to do radical surgical extirpations of the by-passed diseased segments of bowel. In the first operations in this clinic in this series of 223 cases, ileocolostomy was done in only 5 patients.

Surgical treatment, then, consists of radical resection of the diseased intestine together with its mesentery and with all the adjacent lymph nodes that can be removed *en bloc* without interfering with the blood supply to the rest of the colon or small bowel. The criticism has been leveled that this carries with it a higher mortality than a simple ileocolostomy and is a difficult technical procedure.

Attention is called to the group of 18 cases of ileocolostomy done prior to the patient's admission to the clinic. None of these patients had had relief of their symptoms for more than five or six years before coming to the clinic for radical surgical treatment and many of them for much shorter intervals since operation. In many of them distress had continued unabated and even increased (table III).

The mortality in this series of cases in which there were 243 resections was 2.46 per cent (6 deaths). The total number of operations of all types was 269, with 7 deaths in the group or a percentage of 2.6 (table IV). This takes into account in the larger number of operations that many later operations were done for recurrent disease. The causes of death in these 7 patients are listed in table V. Some patients in this group have had from two to four operations in this clinic which were necessary because of recurrent disease.

TABLE IV

Regional ileitis mortality—223 patients

Resections	243
Deaths	6 (2.4%)
Total operations	269
Deaths	7 (2.6%)

TABLE V

Regional ileitis; cause of operative mortality

Operation	Cases	Cause of Death
Resection (extensive)	1	Inanition
Resection	2	Embolism
Resection	3	Peritonitis
Ileocolostomy	1	Sepsis
Total (6 deaths after resection)	7	

TABLE VI

Regional ileitis; primary operation at Lahey Clinic

	Cases
Resection of ileum and colon	174
Resection of small intestine	28
Ileocolostomy (no resection)	5
Entero-enterostomy	3
Laparotomy only	4
Drainage of abdominal abscess	3
Ileostomy	2
Appendectomy	4
Total	223

Garlock has stated that ileocolostomy is a preferable procedure in that there was no operative mortality in a reported series of 57 cases, whereas he reported a mortality of 14 per cent following resection. Certainly, radical resection has a decided advantage in removing diseased bowel—excising any intra-abdominal fistula or fistula to the abdominal wall—and carries with it the hope of more complete eradication of the disease. The technical features of this operative procedure are not difficult and, with very careful delineation of the blood supply and the anatomic structures, the resected loop can be taken out readily without great technical difficulty, and in our experience, without an objectionable increased mortality. Table VI shows the primary operations done at the Lahey Clinic. It will be noted in this series of 223 cases that the primary operation consisted of resection of the ileum and colon in 174 and resection of the small intestine in 28:

in the latter cases there was no involvement of the terminal ileum, cecum or ascending colon. In other words, 202 of the 223 patients had resection. Also, it will be noted that appendectomy was done in 4 patients; this procedure was done in the earlier phase of surgical treatment, before the danger of appendectomy was fully recognized. In view of the large number of fistulas following appendectomy in the presence of regional ileitis, we believe that this operation is highly undesirable and should not be done when such disease exists.

In a previous report from this clinic regarding the recurrence of regional ileitis, Kiefer and associates reported an experience based on 33 patients treated medically and 126 treated surgically. In the group of 33 patients with chronic regional ileitis treated by medical means, 18 were not relieved and surgical treatment was advised. In a study of the results of surgical treatment of 126 patients, 112 were followed carefully; 2 were dead of undetermined causes and 8 were followed for less than 2 years, leaving 102 resected cases with a follow-up record of 2 to 10 years. The recurrence rate in this series of cases was 34 per cent. It was noted, however, that most of the recurrences occurred within 2 years after operation, but the longer the follow-up—it was recognized—the greater the probability of increasing numbers of recurrences. In 1939, Rhoads[7] collected from the literature 125 cases of regional ileitis in which resection had been done. The mortality rate in this series was 8.8 per cent and the incidence of recurrence was 9.2 per cent. Unfortunately, however, the follow-up period in many of these cases was too short to draw definite conclusions. As stated above, these cases must be followed for many years before any opinion can be formed concerning the frequency of recurrence.

In this series of 223 patients who had primary operations in this clinic, 35 have had recurrent disease which necessitated a second operation in the clinic, making an incidence of recurrence of 15.7 per cent as proved by operation. In addition to operative evidence, however, we must take into consideration the evidence of recurrent disease based on clinical and roentgenologic findings, and the previous report from this clinic indicates that this figure probably would be doubled. In the group of 102 cases studied by Kiefer and associates, 43 were diagnosed at operation or suspected, and in about half (21) the diagnosis was confirmed by laparotomy. In the remaining 22 patients the clinical and roentgenologic evidence was so convincing that the diagnosis of recurrent disease seemed quite evident. Again, in this group there were 9 patients who came to a third operation and 2 patients who had 4 operations. Recurrent regional ileitis thus has been confirmed by laparotomy in 35 of the 223 patients operated upon.

Consequently, from our experience with the surgical and medical treatment of regional ileitis in this clinic, a recurrence rate as high as 30 per cent can be anticipated if these cases are followed for 5 to 10 years. Although it is evident that the results of surgical treatment may show a high recurrence rate of the disease it must be conceded that surgical treatment, and preferably resection, is the only method that offers any hope of improvement or relief of this serious pathologic process. Garlock, Crohn, Klein and Yarnis[5] reported that the incidence of recurrence was 10.5 per cent in the group having ileocolostomy with exclusion, but

concluded that the over-all recurrence rate was 22.3 per cent. Bockus,[2] in discussing the paper by Garlock and co-workers, stated that 41 of the 103 patients were either dead or had recurrences, and to him that meant bad results in about 40 per cent of the cases. He stated that if we review the entire group of 137 cases which Garlock and co-workers reported, we find that 75 of their patients were dead or had recurrences or had not been followed-up, so that 55 per cent have had bad or unknown results. He also pointed out that the patients whom he usually had difficulty in following were those who were not well. He emphasized that regional ileitis remains a dread disease and that permanent cure, utilizing either medical or surgical treatment, often is not achieved. He also stated that operation is required in the majority of patients studied on his service.

In tables VII, VIII and IX, operation for recurrence, it may be noted that of the patients who had 2 operations, 2 had permanent ileostomies and total colectomies; of those who had 3 operations there were 3 with permanent ileostomies and total colectomies and of those who had 4 operations there were 2 with permanent ileostomies and total colectomies. Thus, it is apparent that in a few instances the disease process may be progressive and involve the entire colon, and that cure

TABLE VII

Regional ileitis; operation for recurrence. Second operation at Lahey Clinic

	Cases
Re-resection of ileum and colon	28
Entero-enterostomy	3
Permanent ileostomy and total colectomy	2
Ileostomy	1
Ileocolostomy	1
Total	35

TABLE VIII

Regional ileitis; operation for recurrence. Third operation at Lahey Clinic

	Cases
Re-resection of ileum and colon	5
Resection of ileum	1
Permanent ileostomy and total colectomy	3
Total	9

TABLE IX

Regional ileitis; operation for recurrence. Fourth operation at Lahey Clinic

	Cases
Permanent ileostomy and total colectomy	2

or relief ultimately is achieved in a few patients in whom the colon is completely removed, but not even in all of these. In several of these patients, even after complete colectomy, the disease has progressed upward in the small bowel, with repeated massive hemorrhages developing from the disease process in the bowel, ultimately ending in death.

It is our opinion that surgical resection is indicated for all cases of regional enteritis complicated by fistulas, abscesses, obstruction and granulomatous masses, with progressive disease resulting in malnutrition and inanition—in other words, in failure to control the disease by conservative medical methods. The high recurrence rate after resection or after any form of operation indicates that surgery alone has not proved to be adequate and that additional measures are absolutely necessary. We agree with Kiefer that a prolonged postoperative period of medical management is an absolute necessity during which an effort is made to obtain complete rest—and he advises a rest cure of six months or longer with a sanatorium-like treatment—great attention to adequate bodily nutrition, with medication to effect reduction of intestinal motility, close observation to prevent evidence of anemia, and attention to diet to promote the best possible normal intestinal function. In our experience, ACTH and cortisone have in no way affected the progress of this disease, but may improve the nutritional status and sense of well-being of the patient. These drugs are not nearly as beneficial in producing remissions of the disease as they are in ulcerative colitis. In an occasional case of severe, acute, toxic regional ileitis there may be a response to ACTH which will assist in stabilizing the patient's condition and improve nutrition. Antibiotics and sulfonamides as yet have not had any demonstrable effect upon the primary inflammatory process in the intestine and mesentery, and are not specific, but may be used to inhibit secondary bacterial growth. No particular benefit has resulted from their long continued administration.

SUMMARY

We have presented our surgical experience with a series of 223 patients admitted to the clinic for treatment of regional ileitis. The mortality rate following 243 resections was 2.46 per cent and the rate for the entire group of 269 operations was 2.6 per cent. The recurrence rate after surgical treatment in this group of patients was 15.7 per cent, and a recurrence rate of approximately 30 per cent can be anticipated on the basis of clinical and roentgenologic evidence in addition to confirmation by laparotomy.

It is our opinion that radical resection of the diseased bowel is the only method that offers any improvement or complete relief of this disease by eradication of the inflammatory process, fistulas or abscesses, and can be done with a great margin of safety.

REFERENCES

1. Bockus, H. L.: Gastroenterology, Philadelphia, W. B. Saunders Company, 1944, vol. 2, p. 158.
2. Bockus, H. L., in discussion on Garlock, J. H. et al.[5]
3. Crohn, B. B.: Regional Ileitis, New York, Grune and Stratton, 1949, p. 113.
4. Crohn, B. B., Ginzburg, L., and Oppenheimer, G. D.: Regional ileitis; pathologic and clinical entity, J.A.M.A. *99:* 1323 (Oct. 15) 1932.

5. Garlock, J. H.; Crohn, B. B.; Klein, S. H., and Yarnis, H.: Appraisal of long-term results of surgical treatment of regional ileitis, Gastroenterology *19:* 414 (Nov.) 1951.
6. Kiefer, E. D.; Marshall, S. F., and Brolsma, M. P.: Management of chronic regional ileitis, Gastroenterology *14:* 118 (Jan.) 1950.
7. Rhoads, J. E.: Management of regional ileitis and certain other ulcerative lesions of intestines, Pennsylvania M. J. *42:* 1050 (June) 1939.
8. Warren, S., and Sommers, S. C.: Cicatrizing enteritis (regional ileitis) as pathologic entity; analysis of one hundred and twenty cases, Am. J. Path. *24:* 475 (May) 1948.
9. Warren, S., and Sommers, S. C.: Pathology of regional ileitis and ulcerative colitis. (Read before the A.M.A. Section on Gastroenterology and Proctology, New York, June 4, 1953.) To be published.

GASTRIC ULCER AND GASTRIC CARCINOMA

A CORRELATIVE STUDY*

HENRY P. PLENK, M.D.
RU-KAN LIN, M.D.

Salt Lake City, Utah

The number of recent publications dealing with gastric ulcer and gastric cancer is evidence of a renewed interest in the subject. The decrease in mortality after gastric resection during the past 10 years has swelled the camp of those surgeons who advocate routine resection of every stomach displaying a gastric ulcer. The fact that a great many ulcers will heal very promptly on medical management, plus our peculiar emotional attachment to most of our organs, represents a stumbling block to the radical surgical viewpoint. The late Dr. Frank Lahey expressed our dilemma when he said[6]: "I would like to see every gastric ulcer resected and yet I am quite sure if I had one I would not have it resected immediately."

The radiologist plays a vital role in the diagnosis of gastric lesions and in influencing the type of treatment a patient will receive. Once a lesion in the stomach is discovered, the differential diagnosis between benign and malignant lesions is of utmost importance.

The radiologist observes essentially two types of gastric lesions (fig. 1):

1. Space filling.
2. Ulcerative.

1. Benign polyps and polypoid carcinoma belong to this group. However, most malignancies will reduce the lumen of the stomach by diffuse infiltration and thickening of the wall and should be included under this heading. Some of these tumors will reveal superficial ulceration of the mucosa on pathologic examination. Often such ulcers cannot be seen on the roentgenogram. Whether or not an ulcer can be demonstrated is unimportant. The presence of a mass and the reduction of the lumen will lead to the diagnosis of malignancy.

2. Many gastric ulcers will display either an *addition* or a *subtraction* defect. To produce an *additional* defect, the ulcer has to penetrate not only through the mucosa but also through the muscularis. It will appear as a clear cut cavity outside of the regular confines of the stomach. A *subtraction* defect is usually produced by a tumor which grows into the lumen of the stomach. Peptic activity will produce ulceration of the tumor mass. The remaining edge of the tumor will form a meniscus when seen in profile. Figures 2 and 3 reveal examples of these two types of lesions.

The difficulty in diagnosis arises from the fact that a certain percentage of

* From the Dept. of Radiology, University of Utah, St. Mark's Hospital and Salt Lake General Hospital.

Presented during the annual assembly of The Southwestern Surgical Congress, Salt Lake City, Utah, Sept. 21-23, 1953.

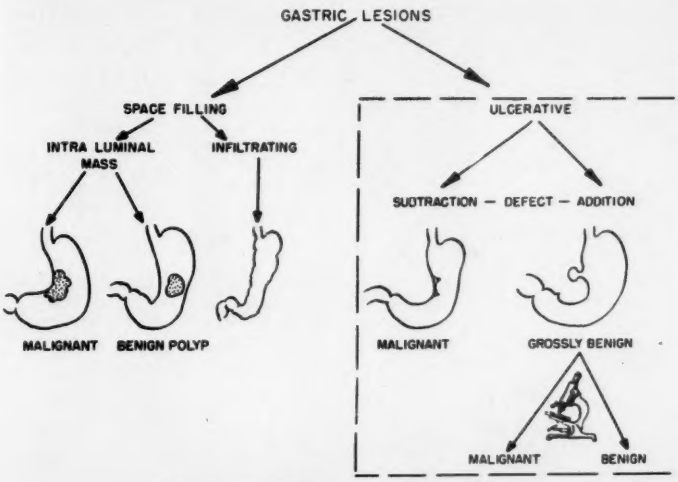


FIG. 1. Classification of gastric lesions

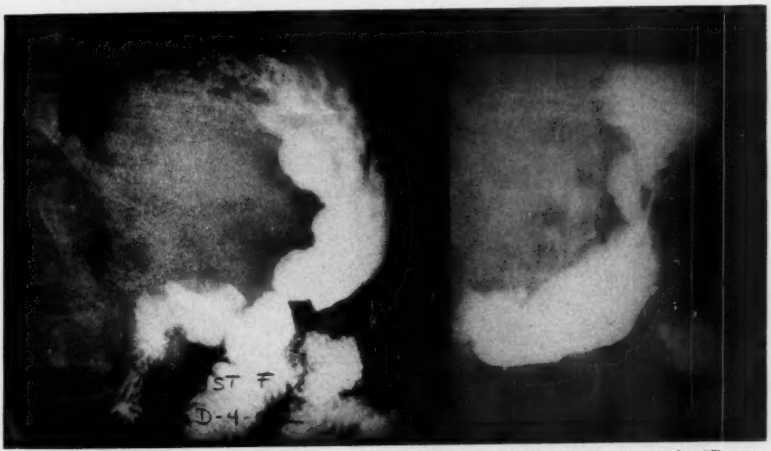


FIG. 2. *Subtraction* defect produced by malignant ulcer of body of the stomach. (Courtesy of Dr. R. M. Crowder.)

ulcers—supposedly indistinguishable from benign lesions—turn out to be malignant when examined microscopically. In the past, these lesions were thought to result from malignant degeneration of a benign ulcer. Wilson and MacCarty[21] reported that 70 per cent of malignant ulcers develop in this manner. Since 1909, the pendulum has swung the other way. In a recent British statistical study, the authors[1] conclude that histologic evidence of malignant change cannot be accepted at face value and that the figures quoted in the literature for the incidence of *ulcer-cancer* are invalid and illusory.

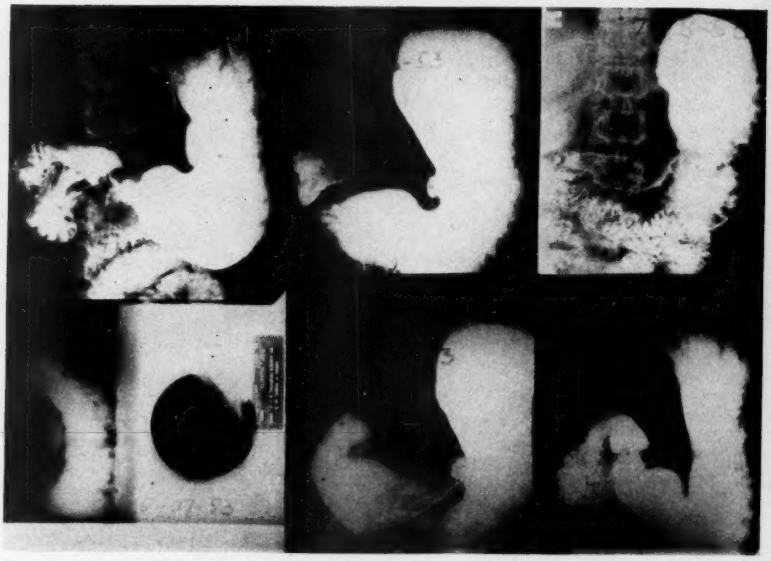


FIG. 3. *Addition* defect produced by large benign gastric ulcer of body with progressive healing. The patient had a laparotomy for diverticulitis six weeks after the last roentgenologic examination and no residual evidence of the ulcer could be detected.

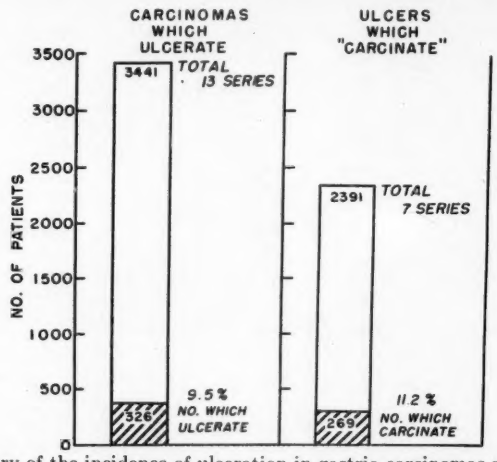


FIG. 4. Summary of the incidence of ulceration in gastric carcinomas and of malignancy in gastric ulcers from the literature.

The reported incidence of ulceration in carcinomas of the stomach as well as the incidence of malignancy in gastric ulcer was reviewed. Information regarding the frequency of ulceration in carcinomas was found in 13 papers published since 1937[2, 3, 4, 5, 8, 12, 13, 14, 17, 18, 19, 20, 22] (fig. 4). Three hundred and twenty-six ulcers were reported in a total of 3,441 resected carcinomas. This represents an

incidence of ulceration of 9.5 per cent. Unfortunately, it is not always apparent whether these ulcers were demonstrated by roentgenogram or by pathologic examination and whether or not they were associated with a mass. The incidence of malignancy in primarily ulcerative lesions was found to be 11.2 per cent or 269 of 2391 cases. Seven recent series published since 1949 were used as the source of our review.[17-23]

MATERIAL

This study comprises a total of 236 gastric lesions observed in four private hospitals, in a charity teaching hospital and in a Veterans Administration hospital. These hospitals represent over two-thirds of the hospital beds in Salt Lake City, Ogden and Provo, Utah. There were 159 benign gastric ulcers and 77 carcinomas. The diagnosis of almost every malignancy was confirmed by pathologic section. A few cases were included in which the roentgenograms and the gross appearance at operation were indicative of malignancy although no positive biopsy was obtained. Only those benign lesions demonstrated by means of roentgenograms were included in which either a pathologic diagnosis was available or when complete healing on subsequent roentgenographic examination, as well as the clinical course of the patient, left little doubt as to the benign nature of the lesion. Sixty-one of the 236 patients had gastroscopic examinations in addition to roentgenographic studies.

FINDINGS

The stomach was arbitrarily divided into five areas (fig. 5): (1) the fundus, (2) the prepyloric area, (3) the greater curvature, including a strip of 2 cm. of anterior and posterior wall between the fundus and the prepyloric area, (4) the body minus the greater curvature and (5) the antrum without the greater curvature.

The distribution of the total number of lesions as well as a breakdown into benign and malignant lesions is seen in figure 5 and in table I.

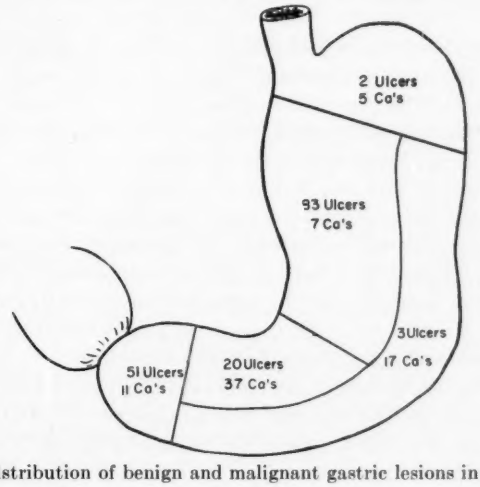


FIG. 5. Distribution of benign and malignant gastric lesions in our series

TABLE I

Distribution of 236 gastric lesions

Location	No. of Lesions	Per cent of Entire Group	Benign Lesions		Malign. Lesions	
			No.	Per cent	No.	Per cent
Fundus	7	2.9	2	28.6	5	71.4
Body without greater curv.	90	38.1	83	92.2	7	7.8
Antrum without greater curv.	57	24.2	20	35.1	37	64.9
Prepyloric area	62	26.3	51	82.3	11	17.7
Greater curvature	20	8.5	3	15.0	17	85.0
Total	236	100.0	159	67.4	77	32.6

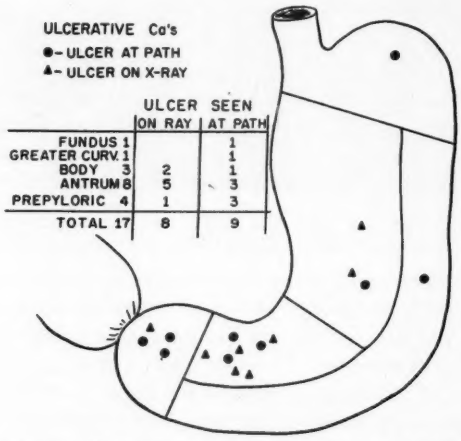


FIG. 6. Incidence and distribution of malignant lesions with ulceration

1. *Fundus:* Seven lesions were located in the fundus. Of these, 5 or 71.4 per cent were malignant, and 2 or 28.6 per cent were found to be benign.

2. *Prepyloric Area:* The prepyloric area was the second most common site for gastric lesions accounting for 62 cases (26.3 per cent). Of these, 51 (82.3 per cent) were benign and 11 (17.7 per cent) were malignant.

3. *Greater Curvature:* The greater curvature of the stomach was one of three areas in which more malignant lesions than benign lesions were found (17 vs. 3).

4. *Body:* The greatest number of lesions in any area, 90 or 38.1 per cent was found in the body. Eighty-three lesions (92.2 per cent) proved to be benign ulcers. Most of these were crowded into the lower half of the body close to the lesser curvature on the posterior wall. The remaining 7 lesions were malignant (7.8 per cent). They were farther away from the lesser curvature.

5. *Antrum:* Fifty-seven cases or 24.2 per cent of all lesions were located in the antrum. Of these, 20 or 35.1 per cent were benign and 37 or 64.9 per cent were malignant. The antrum, then, represents the most common site for malignant lesions in our series.

Of 236 lesions, 167 revealed ulcers on roentgenogram. One hundred and fifty-nine ulcers were benign, 8 were malignant (4.7 per cent). Nine additional ulcers could be seen in the pathologic specimen but were not demonstrable by roentgenogram. All 17 malignant ulcers represented ulcerations in a tumor mass. None was a penetrating ulcer. The 17 malignant ulcers represent 22 per cent of 77 gastric carcinomas. Only 8 carcinomas (10 per cent) revealed ulceration by roentgenogram. The distribution of the ulcerative lesions can be seen in figure 6.

DISCUSSION

We find no convincing evidence that a carcinoma developed from a benign ulcer in any of our patients. A benign gastric ulcer in the region of the angulus coexisted with a prepyloric annular carcinoma in 1 patient. Three patients had two benign ulcers each.

The most striking finding in this study was the fact that no malignant ulcer produced a true addition defect. The body of the stomach is the only area in which such a defect usually can be demonstrated without doubt by spot films in various degrees of obliquity. As a rule, this is not possible in the antrum. Conversely, many cases of benign ulcers will produce *subtraction* defects which are indistinguishable from malignancies. This is particularly true in the presence of inflammation of the gastric mucosa surrounding an ulcer.

A malignant ulcer is a relatively uncommon lesion. The occurrence of carcinoma in a truly penetrating ulcer with a clear cut *addition* defect is so uncommon that we did not find a single case in our material. The statistical accuracy of roentgenographic diagnosis in ulcer of the body and lesser curvature, almost regardless of size, is many times greater than with lesions in the antrum, prepyloric area, the fundus or the greater curvature.

Since many gastric ulcers will heal very promptly, we believe that any lesser curvature ulcer between the angulus and the cardia, displaying a true *addition* defect, can be considered benign until proved otherwise. Such a patient should not be subjected to routine surgical resection in the absence of other indications for operation. However, if strict medical management for three weeks does not produce a decrease in size, and a complete healing has not resulted in six to eight weeks, gastric resection should be done.

The differential diagnosis in the distal portion of the stomach is much more difficult. Many more patients with lesions in this area will require early exploration and resection. Many benign ulcers will need to be resected to avoid unnecessary delay in the treatment of one carcinoma. In fact, we should expect to explore some patients in whom no adequate explanation for the presence of minor but persistent roentgenographic findings can be made.

SUMMARY AND CONCLUSIONS

Two hundred and thirty-six cases with gastric lesions were reviewed. One hundred and fifty-nine, or 67.4 per cent were benign ulcers, and 77 or 32.6 per cent were carcinomas.

Seventeen or 22 per cent of 77 carcinomas ulcerated. Only 8 (10 per cent) of these ulcerations were seen on the roentgenogram.

Four and seven-tenths per cent (8 cases) of 167 ulcerative lesions demonstrable by roentgenogram were proved to be carcinomas. In none of these was a true addition defect present. No case of *malignant degeneration* of a benign ulcer was found.

The accuracy of the roentgenographic diagnosis of benign ulcers along the lesser curvature of the body is very high if a true addition defect is present.

Surgical exploration and resection has to be used if the ulcer does not heal regardless of the roentgenographic appearance.

Roentgenographic diagnosis is much less reliable in antral or prepyloric lesions, and earlier exploration is required in many more lesions in this area.

We express our appreciation to Drs. H. J. Brown, Provo, Utah, L. P. Matthei, Ogden, Utah, R. R. Meyer and A. K. Wilson, Salt Lake City, whose kind help has made this study possible.

REFERENCES

1. Beattie, A. D., and Moroney, M. J.: "Ulcer-cancer" of stomach, Brit. J. Cancer *6:* 215 (Sept.) 1952.
2. Boman, K., cited by Ekström, T.[3]
3. Ekström, T.: On development of cancer in gastric ulcer and ulcer symptoms in gastric cancer, Acta chir. Scandinav. *102:* 387 (Jan.) 1952.
4. Hedly, I., cited by Ekström, T.[3]
5. Jemerin, E. E., and Colp, R.: Gastric carcinoma; statistical study based on three hundred and forty-four cases from 1938 through 1947, Surg., Gynec. & Obst. *95:* 99 (July) 1952.
6. Lahey, F. H., in discussion on Brown, C. H., and Kane, C. F.: Carcinoma of stomach; review of four hundred and six cases seen from 1940 to 1945; operability, resectability and curability, Gastroenterology *22:* 64 (Sept.) 1952.
7. Lampert, E. G.; Waugh, J. M., and Dockerty, M. D.: Incidence of malignancy in gastric ulcers believed preoperatively to be benign, Surg., Gynec. & Obst. *91:* 673 (Dec.) 1950.
8. Landelius, E.: Results of partial and total gastrectomy in cancer of stomach, Acta chir. Scandinav. *96:* 441, 1947/48.
9. Malmros, H., and Hiertonn, T.: Post-investigation of six hundred and eighty-seven medically treated cases of peptic ulcer, Acta med. Scandinav. *133:* 229, 1949.
10. Marshall, S. F.: Relation of gastric ulcer to carcinoma of stomach, Ann. Surg. *137:* 891 (June) 1953.
11. Milstein, B. B.: Late results of partial gastrectomy, Ann. Surg. *133:* 1 (Jan.) 1951.
12. Ochsner, A., and Blalock, J.: Carcinoma of stomach; necessity for reevaluation of therapeutic philosophy, J.A.M.A. *151:* 1377 (April 18) 1953.
13. Pförtner, W., cited by Ekström, T.[3]
14. Schindler, R.: Relative surgical curability of certain gross types of gastric carcinoma, Surg., Gynec. & Obst. *83:* 453 (Oct.) 1946.
15. Smith, F. H., and Jordan, S. M.: Gastric ulcer; study of six hundred cases, Gastroenterology *11:* 575 (Nov.) 1948.
16. Stevenson, C. A., and Yates, C. W.: Accuracy of roentgen diagnosis of benign gastric ulcer, Radiology *52:* 633 (May) 1949.
17. Stewart, M. J.: Cancer of stomach; some pathological considerations, Brit. J. Radiol. *20:* 505 (Dec.) 1947.
18. Swynnerton, B. F., and Truelove, S. C.: Simple gastric ulcer and carcinoma, Brit. M. J. *2:* 1243 (Nov. 24) 1951.
19. Thorgersen, E., cited by Ekström, T.[3]
20. Walton, J.: Carcinoma of stomach, Brit. M. J. *2:* 1127 (Dec. 9) 1939.
21. Wilson, L. B., and MacCarty, W. C.: Pathological relationships of gastric ulcer and gastric carcinoma, Am. J. M. Sc. *138:* 846, 1909.
22. Wulff, H. G.: Über das Vorkommen von Ulcuscarcinom und Carcinom im Ulcusmagen, Acta chir. Scandinav. *80:* 433, 1938.

MANAGEMENT OF PANCREATIC CYSTS AND PANCREATIC LITHIASIS

CHARLES B. PUESTOW, M.D.*
WILLIAM J. GILLESBY, M.D.†

Chicago, Ill.

Pancreatic cysts and pancreatic lithiasis are rather common complications of chronic recurring pancreatitis. This presentation is an analysis of 45 cases of pancreatic cyst and 23 cases of pancreatic lithiasis with intractable pain.

Gambill[7] has stated that pancreatic calcification may appear in approximately 33 to 50 per cent of cases of relapsing pancreatitis. The inclusion of all pancreatic cysts under the diagnosis of chronic recurring pancreatitis is open to question. Chronic recurring pancreatitis may be said to be a summation of repeated attacks of acute pancreatitis (Richman and Colp[13]).

It has been fairly well established that the inflammatory process may be initiated by preventing the external secretion of a stimulated gland from entering the duodenum (Lium, and Maddock[10]). The large number of theories advanced as possible causes of chronic recurring pancreatitis bring to mind a statement by an unknown author that "a multiplicity of explanations denotes a paucity of facts". Spasm of the sphincter of Oddi and increased stimulation of the gland may be caused by the ingestion of ethyl alcohol. Muether and Knight[12] pointed out that carbonated beverages and alcohol are apparently responsible for the exacerbation of symptoms in many cases. In analysis of our cases we have noted that with almost no exceptions the patients were alcoholic addicts and of the lower strata of society. They admit regular drinking of large quantities of cheap beverages which may be assumed to have been adulterated. Bennett[1] et al, stated that methanol (wood alcohol, methyl alcohol) poisoning is often associated with elevated amylase levels and on autopsy cases of acute pancreatitis are found. It is known that methanol and ethyl alcohol in combination are not as poisonous as methanol alone. The ethyl alcohol inhibits methanol breakdown. The contents of methanol in cheap liquors ranges from 0 to as high as 5 per cent, depending on the degree of adulteration of the liquor with denatured alcohol or other adulterants. We believe that the regular consumption of methanol containing liquors may produce pancreatitis, which is of a subacute type and permits the patient to survive to chronicity with exacerbations following each drinking episode.

In our series several patients admitted drinking *smoke* which may be as high as 5 per cent methanol in content. Apparently, the detoxification of *smoke* is accomplished by different methods in different parts of the country and we

* Chief, Surgical Service, Veterans Administration Hospital, Hines, Illinois. Clinical Professor of Surgery, University of Illinois College of Medicine, Chicago, Illinois.
† Assistant Chief, Surgical Service, Veterans Administration Hospital, Hines, Illinois.
Presented during the Southwestern Surgical Congress fifth annual assembly, Salt Lake City, Utah, September 21–23, 1953.

were amazed to find that the patients we questioned knew all of the tricks. For instance, *smoke* was detoxified by the filtration of denatured alcohol through a loaf of bread in Atlanta, by the mixing with water and some form of filtering in Philadelphia, and by another method reported from Seattle. Brown and Harvey[4] have observed spontaneous hypoglycemia in *smoke* drinkers. This could be due to pancreatitis irritating the islet tissue and producing hyperinsulinism.

In our cases we have found almost all of the cysts to be of the pseudocyst type. It is believed that pseudocyst formation is due to rupture of a duct as a result of increased intraductal pressure with secondary digestion and effusion of pancreatic juice into surrounding tissues. This effusion may be limited to the pancreatic tissue or it may find its way into the lesser peritoneal cavity or, in some cases, into the entire peritoneal cavity. Chemical peritonitis is the result. The peritoneum, in walling off this fluid, forms a cyst which does not have an ordinary cyst wall, but the structures in the vicinity of the cyst become the wall of the cyst. The cyst fluid is a mixture of pancreatic juice containing high levels of amylase and lipase and possibly some partially digested material. The color of the fluid may be clear or of a muddy, brownish appearance. Occasionally, it may contain greenish material which probably is evidence of bile admixture. The cyst usually is in communication with one of the pancreatic ducts. In the past, the treatment of pancreatic cysts generally has been that of marsupialization. The pancreas produces from 1000 to 2000 cc. of fluid daily. This fluid is similar to plasma in its electrolyte content, but has very little protein. If the cyst is treated by marsupialization the cyst fluid is regularly lost and if the fistula persists there is a loss of electrolyte containing fluid daily for many months. If the cyst is badly infected it is sometimes necessary to treat it by marsupialization. However, we believe that the cyst fluid should be returned to the body in some way, and hence, are advising internal drainage. Removal of cysts is rarely possible as the cysts are not clearly defined and have no well defined pedicles. The bases of these cysts are generally located over the surface of the pancreas and complete removal of the cyst wall is impossible. In 1 case in our series it was possible to remove the cyst, but the spleen formed part of the cyst wall so that splenectomy

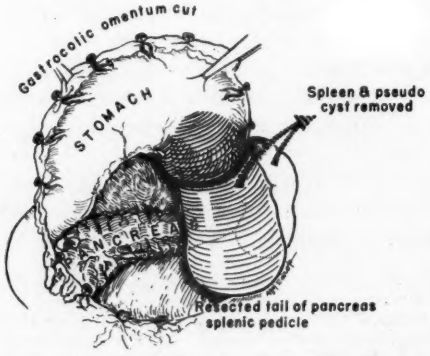


FIG. 1. Resection of pseudocyst, spleen and tail of pancreas

FIG. 2. Pseudocyst of the pancreas with effusion in the left pleura. It is clearly distinct from the stomach. The air was accidentally admitted into the cyst during aspiration. Other films showed diffuse calcification of the pancreas.

and resection of the tail of the pancreas was necessary.[14] If it is technically possible to anastomose the cyst of the pancreas to any region of the stomach or small bowel, it probably is best to do such an anastomosis. We have had 4 cases in which cystogastrostomy[3] was done and in none of these cases has there been retention of food or foreign material in the cyst cavity.

We believe that the procedure of choice in cases of cyst of the body of the pancreas is a Roux Y cystojejunostomy the technic of which is shown in figure 3. If the cyst is present in the head of the pancreas we have utilized the Roux Y anastomosis, figs. 4 and 5. In 1 case an interesting preparation was made before draining the cyst (fig. 6). A duodenal ulcer with some obstruction was present at the pylorus. It was believed that a gastric resection should be done and it seemed feasible that a cystoduodenostomy uniting the cyst to the open end of the duodenum would adequately drain the cyst. These operations were done. It was then decided to do a cholecystoduodenostomy to drain the biliary tract. Thus, this patient had biliary tract drainage, adequate drainage of the pancreatic cyst, and gastric resection as advocated by Richman and Colp.[13] Gastric resection is believed to decrease the secretion of the pancreas and relieve the pain of chronic pancreatitis. Unfortunately, this patient's pain persisted just as before and it was necessary to do a left thoracolumbar sympathectomy and splanchnicectomy to relieve his pain. He has been pain free for approximately a year and is now doing very well.

Approximately a third of our cases of pancreatic pseudocyst also presented pancreatic lithiasis or calcifications (figs. 7 and 8). The patient with pancreatic calcification, (and we believe that this is a better term than lithiasis), had severe

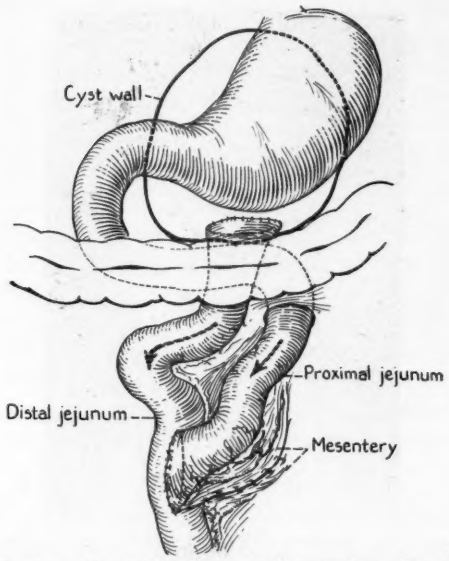


FIG. 3. Drainage of pancreatic cyst by the Roux Y procedure. (Reproduced with permission from "Surgery of the Biliary Tract, Pancreas, and Spleen by Charles B. Puestow, M.D., Chicago Year-Book Publishers, Inc. 1953.)

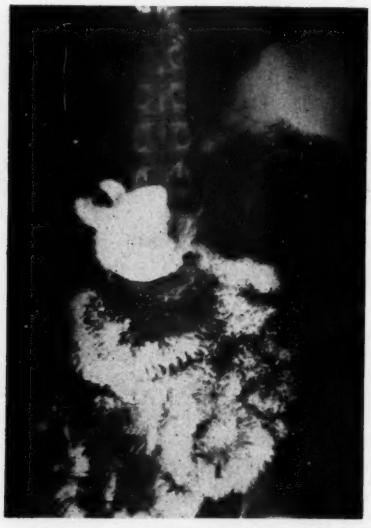


FIG. 4. Roentgenogram showing cyst pressing on the under surface of the stomach. This patient was treated by the Roux Y principle.

FIG. 5. Partially oblique roentgenogram showing the cyst pushing the stomach forward. Same patient as figure 4.

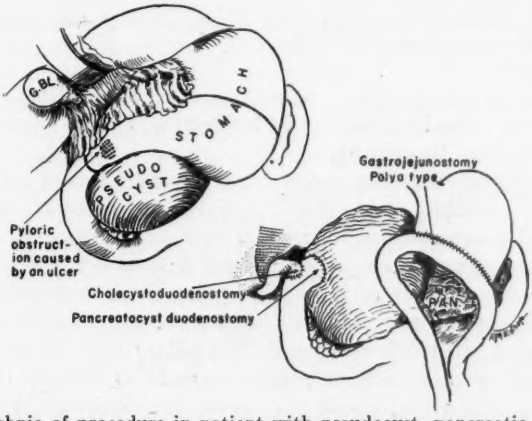


FIG. 6. Technic of procedure in patient with pseudocyst, pancreatic lithiasis and obstructing duodenal ulcer.

pain. It is believed that the calcification does not necessarily occur in the ducts, and we agree with Comfort[6] that the calcification is not a cause of pancreatitis but rather a result of the disease. In most cases of pancreatic calcifications, the calcification is found throughout the gland and is not limited to the duct areas. The calcification probably is due to saponification and subsequent calcification of the soaps in the pancreatic tissue and is not limited to the duct area. In only 1 of our cases of pancreatic cyst was a stone found in the pancreatic duct. On removal of this stone the cyst drained into the duodenum normally. Removal

FIG. 7

FIG. 8

FIG. 7. Lateral view of pancreatic calcification. The calcification in the lower lumbar area is due to phlebolith calcification.

FIG. 8. Diffuse calcification of the head of the pancreas which is shown to be clearly distinct from the gallbladder as visualized by dye. P-A view.

of the stone plus marsupialization was sufficient to relieve this patient of his symptoms. His cyst closed rapidly and he has been well of his pancreatic symptoms for approximately three years.

If lithiasis is marked and fibrosis very extensive and a *burned out* pancreas is present, the best procedure probably is a partial pancreatectomy. It is unfortunate that partial pancreatectomy is delayed until many patients have become narcotic addicts. Perhaps if the procedure were done earlier, the results would be better. The management of intractable pain, either with calcification or without, has brought out many methods and we will present what we believe is the best method in our hands at present. The biliary tract should be drained first. The method we are using at present consists of cholecystectomy and choledochostomy with a long period of common duct drainage. We do not believe that sphincterotomy is indicated[8] and we do not believe that the long T tube extending into the duodenum is a good method. It has seemed to us that the long limb of the T tube may obstruct the pancreatic duct even more if there is a common opening into the duodenum. If the pain is not relieved by this method we use a continuous epidural injection to estimate whether the pain can be relieved by any of the nerve section procedures. We believe this is better than bilateral splanchnic block, but use both methods, depending upon the desires of the anesthesiology department. If relief is obtained from continuous epidural block, we consider a splanchnicectomy and sympathectomy on the side of the pain (fig. 9). This generally has been the left side and in our hands we have de-

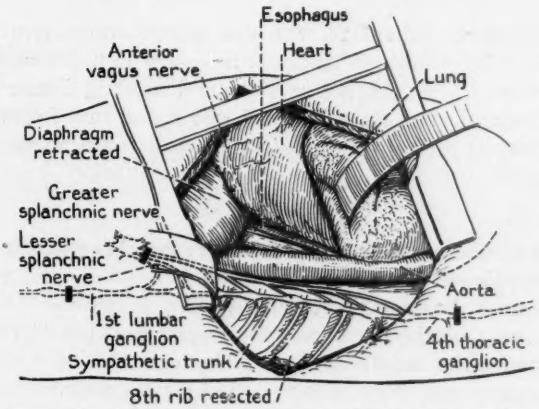


FIG. 9. Left thoracolumbar sympathectomy and splanchnicectomy for relief of pancreatic pain. (Reproduced with permission from "Surgery of the Biliary Tract, Pancreas, and Spleen by Charles B. Puestow, M.D., Chicago Year-Book Publishers, Inc., 1953.)

cided that a transthoracic approach through the eighth rib and resecting the sympathetic ganglia from the fourth thoracic down to and including the first lumbar, including the splanchnic nerves and a portion of the celiac plexus, is the best procedure. We have chosen this method because of disappointment with splanchnic resections of more limited extent. Subdiaphragmatic splanchnicectomy as advocated by Mallet-Guy[11] has provided relief for some of these patients but only for short times. The procedure as advocated by Peet likewise has been of transitory benefit. We have not been impressed by the favorable results of vagotomy in this condition. Dragstedt[6] has also been disappointed with the results of vagotomy in chronic recurring pancreatitis. If the left sympathectomy fails to accomplish its purpose, a right sympathectomy may be done in about two weeks. In analysing the persistent case which cannot be relieved by the above procedures, it is of interest that a recent publication from the Mayo Clinic by Hollinshead[9] pointed out that some of the sensory nerves of the pancreas may arise directly from the cord rather than from the sympathetic chain. In these cases it is believed that partial pancreatectomy is indicated inasmuch as individual nerve section is not feasible in any other manner.

Common duct anastomosis to the jejunum by the Roux Y procedure for the treatment of chronic pancreatitis as advocated by Bowers,[2] has been of value in his cases, but we have not been convinced that it is a physiologic procedure. The occurrence of a duodenal ulcer following side-tracking of the bile from the duodenum has occurred in 3 patients with fatal hemorrhage and we have been recently informed of another case. The presence of bile in the duodenum is necessary to counteract the acidity of the gastric inflow and diverting this stream may be an unphysiologic procedure. If choledochojejunostomy by the Roux Y principle is used, we believe, at present, that a partial gastrectomy should be done at the same time to prevent gastric secretion entering the duodenum without any buffering bile to prevent peptic ulcer.

In those unfortunate individuals with this disease who receive no relief by any of the above procedures, it has been necessary in a few cases to advise unilateral cordotomy. That this is a painful and distressing disease is evidenced by a recent communication from Tidrick[15] who stated that follow-up of their cases showed that 10 per cent of the cases of chronic recurring pancreatitis had committed suicide.

SUMMARY

Methanol in adulterated liquors is considered a possible etiologic agent in the causation of chronic recurring pancreatitis.

Internal drainage of pancreatic cyst is the best treatment.

Chronic recurrent pain in chronic pancreatitis may be relieved by transthoracic splanchnicectomy and sympathectomy.

Partial pancreatectomy may be indicated in certain cases.

REFERENCES

1. Bennett, I. L., Jr.: Nation, T. C., and Olley, J. F.: Pancreatitis in methylalcohol poisoning, J. Lab. & Clin. Med. *40:* 405 (Sept.) 1952.
2. Bowers, R. F.: Surgical therapy for chronic pancreatitis, Surgery *30:* 116 (July) 1951.
3. Brandenburg, F. H.; Maddock, S., and Schweitzer, R. J.: Cystogastrostomy: treatment of pancreatic pseudocysts, Ann. Surg. *133:* 219 (Feb.) 1951.
4. Brown, T. M., and Harvey, A. M.: Spontaneous hypoglycemia in "smoke" drinkers, J.A.M.A. *117:* 12 (July) 1941.
5. Comfort, M. W.: Chronic relapsing pancreatitis, Proc. Staff Meet., Mayo Clin. *22:* 548 (Nov. 26) 1947.
6. Dragstedt, L., quoted by McCleery, R. S.; Kesterson, J. E., and Schaffarzick, W. R.: Clinical study of effect of vagotomy on recurrent acute pancreatitis, Surgery *30:* 130 (July) 1951.
7. Gambill, E. E.: Chronic relapsing pancreatitis (Editorial), Surg., Gynec. & Obst. *92:* 759 (June) 1951.
8. Gray, S. H.; Probstein, J. G., and Sachar, L. A.: Chronic cholecystitis produced by division of sphincter of Oddi, Arch. Surg. *59:* 1007 (Nov.) 1949.
9. Hollinshead, W. H.: Anatomic pathways for pain from upper part of abdomen, Proc. Staff Meet., Mayo Clin. *28:* 385 (July 29) 1953.
10. Lium, R., and Maddock, S.: Etiology of acute pancreatitis; experimental study, Surgery *24:* 593 (Oct.) 1948.
11. Mallet-Guy, P., and de Beaujeu, M. J.: Treatment of chronic pancreatitis by unilateral splanchnicectomy, Arch. Surg. *60:* 233 (Feb.) 1950.
12. Muether, R. O., and Knight, W. A., Jr.: Chronic recurrent pancreatitis. I. Clinical and laboratory aspects, Gastroenterology *12:* 24 (Jan.) 1949.
13. Richman, A., and Colp, R.: Chronic relapsing pancreatitis treatment by subtotal gastrectomy and vagotomy, Ann. Surg. *131:* 145 (Feb.) 1950.
14. Smith, E. B.: Hemorrhagic ascites and hemothorax associated with benign pancreatic disease, A.M.A. Arch. Surg. *67:* 52 (July) 1953.
15. Tidrick, R. T.: Personal communication to the authors.

PERITONEAL TAP AS AN AID IN THE DIAGNOSIS OF ACUTE ABDOMINAL DISEASE

Wm. H. Moretz, M.D.
Wm. G. Erickson, M.D.

Salt Lake City, Utah

Peritoneal tap is a valuable aid in the diagnosis of acute abdominal disease, but it has not been used as generally as it deserves to be. The purpose of this paper is to point out the indications, safety and usefulness of the procedure and to elaborate upon the diagnostic features of the aspirated fluid.

A very thin film of fluid normally covers the peritoneal surfaces within the abdomen. With each of the common causes of acute surgical disease of the abdomen, the quantity of this fluid increases and its characteristics are altered. The altered fluid characteristics have been studied by Steinberg [11, 12] and Coller,[2] but more from the standpoint of peritoneal response to various types of insult than specifically as an aid to diagnosis.

Our interest in the method has been aroused and maintained by the frequency with which the characteristics of the peritoneal fluid give invaluable aid in differentiating between the various causes of abdominal pain. The gross characteristics of the peritoneal fluid, noted on opening the abdomen, frequently suggest the nature of the acute condition, but relatively few surgeons take preoperative advantage of this fact when trying to decide whether or not laparotomy is indicated. That is the time when this information would be of greatest value.

A peritoneal tap is not needed in everyone with abdominal pain. Many such patients have symptoms and signs sufficiently clear to establish the diagnosis, or the need for laparotomy, beyond a reasonable doubt. However, there are some patients in whom the diagnosis and the need for laparotomy is uncertain. For these borderline cases the diagnostic peritoneal tap frequently is of great value.

OBSERVATIONS

Dangers. Since the type of fluid present in the abdominal cavity can be of such diagnostic help, why has there not been a more general acceptance of this procedure? The one thing, more than any other, which has prevented its acceptance is the inherent fear that a needle inserted into the abdomen very likely will penetrate the bowel and cause leakage of its contents into the peritoneal cavity. There are two excellent reasons why this fear is unwarranted. In the first place —although it is true that the point of the needle usually will touch one or more loops of intestine—the needle rarely will penetrate the bowel unless the bowel is so fixed that it cannot slip out of the way. Even when the intestine is im-

From the Department of Surgery, University of Utah College of Medicine and Salt Lake General Hospital, Salt Lake City, Utah.

Presented during the annual assembly of The Southwestern Surgical Congress, Sept. 21-23, 1953, Salt Lake City, Utah.

mobilized by dense adhesions, the needle can be inserted into its lumen only with difficulty. In the second place, even if the needle can be made to enter the intestine, no harm results.

We purposely have run needles of various sizes into the bowel wall at operation and invariably have noted that there is no significant leakage of intestinal contents from the puncture wound after the needle is withdrawn. This was true even when a no. 13 needle was inserted into a loop of obstructed ileum, distended to three times its normal size. Occasionally, a few drops of blood may ooze from the puncture site, but this ceases within a few minutes and never results in any significant blood loss. Neuhof and Cohen,[9] in an experience with more than 100 taps, did not observe a single instance of injury to the intestine. The safety of the procedure has been emphasized by all who use it, but still a fear exists.

Several simple experiments were carried out to demonstrate the safety of the peritoneal tap.

1. Thirty intravenous needles, sizes 20 to 15, were inserted indiscriminantly through the abdominal wall into the peritoneal cavity of a small, anesthetized, female dog. The abdominal wall was then turned down as an apron after being detached superiorly and laterally. A careful examination of the entire bowel revealed no evidence of a needle having entered it, except in the lower rectum where three puncture wounds could be seen. This part of the rectum was relatively fixed and so full of semisolid feces that it filled the entire anteroposterior diameter of the pelvis and could not move away from the needles. No such relationship exists in the human being in any of the recommended sites for tapping. In spite of the three puncture wounds, no leakage was visible. This experiment demonstrated the ease with which normal mobile bowel evades injury from a needle inserted through the abdominal wall.

2. Further tests were made to determine whether or not harm results even if a needle does pierce the bowel wall. The entire small and large bowel of the above dog was excised and ligated distal to the three rectal puncture wounds. The specimen was fully distended by admitting air under pressure through the duodenum. No leakage of air occurred, checked by having the bowel under water, even when the specimen was ballooned out by a pressure of 120 mm. of Hg., exceeding by far any conceivable pressure which might exist clinically. The usual intraluminal pressures observed in the presence of complete obstruction are less than 20 mm. of Hg. for the large bowel and less than 15 mm. of Hg. for the small bowel.[14]

3. The abdominal cavity of an anesthetized dog was opened, and closed; 10 inch long loops of jejunum, ileum and colon were created by ligating the intestinal segments at each end with heavy cotton thread. Five needles, sizes 18 and 20, were inserted into each loop. These needles were withdrawn and each loop was inflated under water to a pressure of 100 mm. of Hg. No leakage occurred in any loop. Not until pressures of 350 mm. of Hg. (colon), 280 mm. of Hg. (ileum), and 260 mm. of Hg. (jejunum) were reached, did air escape through the puncture wounds.

4. Representative areas of ileum, jejunum and colon were also tested in a

living dog as follows: a no. 15 needle, attached to a continuous source of air under 100 mm. of Hg. pressure, was attached to a closed segment of bowel. While the segment was thus distended with a pressure of 100 mm. of Hg., a no. 20 needle was inserted and withdrawn. The segments partially deflated as air escaped through, but not around, the no. 20 needle. In each instance, as soon as this needle was withdrawn, no further escape of air occurred and the segment immediately became reinflated to the original pressure of 100 mm. of Hg. This test was repeated many times in each part of the intestine, the no. 20 needle being inserted at different angles, varying between 15 and 90 degrees to the surface of the bowel. The results invariably were the same—no leakage. By putting great traction on a loop of colon, we were able to get a fresh puncture wound to leak at 35 mm. of Hg., and by making a puncture wound in a partially devitalized segment of jejunum, leakage occurred at 55 mm. of Hg.

These experiments and our clinical experience have convinced us that the diagnostic peritoneal tap is a safe procedure.

Precautions. To supplement the inherent safety of the procedure, several precautions are to be observed. The inferior epigastric vessels should be avoided by selecting a site away from their course. Either of the lower quadrants or the lower midline may be used with safety. The solid structures—the kidneys, spleen and liver—are thereby avoided. The bladder should be empty, especially if the midline is to be used. We elect to insert the needle near, but not directly into, the site of suspected disease, even though Steinberg and Martin[13] demonstrated an early generalized peritoneal reaction following perforations. Previous operative scars are avoided since the likelihood of adhesions fixing the intestine in those areas is greater. Marked distention of the bowel may be a relative contraindication, although we have used the procedure in such instances and have seen no untoward effects. We elect to do the tap away from the distended loops of bowel.

Technic. Preferably, the tap is done after the patient has been lying on his side for a few minutes with the site to be used in a dependent position. This probably will make the fluid more easily obtainable, if only a small quantity of fluid is present. The needle may be inserted with the patient still on his side or immediately after he resumes the supine position. The skin is prepared in any acceptable manner. No draping is required, nor is it necessary to wear sterile gloves. We prefer to use a no. 18 spinal puncture needle, about 2 inches long, with a smooth, relatively blunt point and with the stylet in place. Procaine hydrochloride 1 per cent may be used in the skin and even along the future path of the needle down to the peritoneum, but, generally, no local anesthesia is required. The needle is inserted perpendicular to the skin surface, until its point is thought to be several millimeters within the peritoneal cavity. A *snap* or *give* usually can be felt as the needle passes the thick, anterior muscular fascia, and another as the needle passes the thick, posterior muscular fascia. Occasionally the peritoneal layer can be felt as a separate, less pronounced *snap*.

With the needle held in place, the stylet is removed and a 10 cc. syringe is attached to the needle. *Gentle* suction is applied and, if fluid flows easily, the syringe is filled and the needle withdrawn. If fluid is not obtained easily, then,

with the syringe still attached, the needle may be inserted further, withdrawn slightly, rotated, or slanted so that its point is thought to lie just beneath the parietal peritoneum. Further suction usually will be productive of at least a few drops of material if any free fluid is present. Even if no fluid enters the syringe, the needle contents should be emptied onto a glass slide for microscopic study. Very frequently, what was thought to be a negative tap thus will reveal pus cells or bacteria, or both, and will be of considerable value.

Most of the procedures have been done with an ordinary no. 18 or no. 20 needle, without a stylet, attached to the syringe while being inserted. This is satisfactory, but the use of a needle with stylet is recommended for two reasons. Unless a stylet is used the needle occasionally becomes plugged by fat or other soft tissue as it penetrates the abdominal wall. The stylet also prevents, to a large extent, the contamination of the peritoneal fluid by red blood cells which otherwise may enter the needle as it is being inserted.

Examination of the fluid. Our routine study of the fluid thus obtained has included the following:

1. Gross characteristics (color, odor, viscosity).
2. pH (nitrazine paper).
3. Free and total acid (Töpfer Method).
4. Smear (Wright's stain, Gram stain and unstained) for cells and bacteria.
5. Culture.
6. Quantitative amylase determination.

In many of our patients complete studies were not made because of an insufficient quantity of fluid, or because the gross characteristics of the fluid made some of the tests unreliable—(such as bloody fluid interfering with the analysis for free and total acid),—or because the specific problem was answered by only one or two of the fluid characteristics. If only a drop or two of fluid was obtained, a smear was examined since this most likely was to give the desired information. In other instances, when gross pus was found, no further studies were made, since the presence of peritonitis was thus proved. The finding of bloody fluid in some patients indicated that the loop of obstructed bowel had become strangulated, making further studies unnecessary. Many of the studies were supplemented by observations on the fluid obtained at operation.

Experience upon which this report is based. This report is based on our experience with this procedure over the past four years, during which time the peritoneal fluids from 75 patients have been examined. Fifty-seven of the specimens of fluid were obtained by abdominal tap, the others being obtained during operation. In 11 patients, no taps were made, the fluid being obtained at operation only. In 7 patients, free fluid was found at operation after *false negative* taps. In 16 additional patients, *true negative* taps were obtained. By *true negative* is meant that no fluid was obtained by the tap, and, either a subsequent operation revealed no fluid (8 patients), or the course of the patient was such that no fluid was likely to have been present (8 patients). One patient had multiple taps, and another, who almost certainly had free fluid, had an unconfirmed *false negative* tap. The total number of abdominal taps was 91, including 2 *false positive* taps.

Complications encountered. In the 91 taps no serious complication has occurred as a result of the procedure. In 2 there was slight bleeding externally from the puncture site, with prompt control by local pressure. The lumen of the bowel was entered four times, the small bowel twice and the large bowel twice. Entrance into the lumen of the intestine by the needle was certain, since typical bowel contents were obtained. In none of these 4 patients—each of whom was later explored—could the puncture site in the bowel wall, or any evidence of leakage, be found. The peritoneal fluid in each of these 4 patients was entirely different from the material aspirated from the bowel lumen. Twice, pure pus was obtained from walled off abscesses and, once, a large renal cyst was entered. Not once was the procedure thought to have been detrimental to the patient.

Gross characteristics of peritoneal fluid. The 73 specimens of fluid—the gross appearances of which were described in the patient's records—are classified under the headings of (a) bloody, (b) purulent, (c) greenish, and (d) others including straw, yellow, milky, turbid, amber, and yellowish brown—in tables I and II.

The fluids usually had no particular odor except in cases of peritonitis wherein E. Coli was an important contributor to the infection. *Foul*, or *fecal* odor was noted in most of the patients with peritonitis from a perforated appendix or sigmoid and from 1 patient with peritonitis secondary to a gangrenous loop of jejunum. The odor was described as *musty* in another patient who had peritonitis secondary to a gangrenous loop of small bowel.

Thick pus was present in many patients who had late peritonitis. Some of the grossly bloody fluids were more viscid than others. Those from free, intra-abdominal bleeding resembled whole blood in viscosity while the red fluid of early strangulation was more watery. Gross particles of food occasionally were observed in fluids from perforated ulcers.

Microscopic findings. Some of the fluids were not examined microscopically. Often, the fluid's gross appearance sufficed to indicate the need for operation and served as a good guide to the kind of disease to expect. The smears usually were made by the intern or medical student, and some descriptions were incomplete or of doubtful accuracy, especially regarding the type of bacteria. Our chief reliance microscopically, was upon the relative numbers of white blood cells and red blood cells in the smear and upon the presence or absence of bacteria. The bacteria usually were present classified as bacilli or cocci and as gram-positive or gram-negative.

Table III contains generalizations drawn from microscopic studies. Much valuable information probably could be gained from a more detailed microscopic study. In this table it is obvious that the polymorphonuclear cells were most numerous with peritonitis, but also were conspicuous in those with acute appendicitis and pancreatitis. They were present in significant numbers in most of the fluids, except those with frank hemorrhage, serositis or early small bowel obstruction. Red blood cells were most numerous in those with frank intra-abdominal hemorrhage, carcinomatosis, bowel infarction and acute hemorrhagic pancreatitis. The few red blood cells which frequently were seen in almost any

TABLE I

Diagnoses associated with 17 grossly bloody fluids

Diagnosis	Appearance of Whole Blood	Reddish-Brown	Serosanguinous
Rupture of solid organ (spleen, kidney, spleen and liver)	3	—	—
Rupture of ectopic pregnancy	2	—	—
Rupture of omentum	1	—	—
Rupture of aneurysm (iliac artery)	1	—	—
Perforation of peptic ulcer	1*	—	—
Carcinomatosis	1*	—	—
Acute pancreatitis (relatively severe)	—	1	—
Infarcted bowel	4	2	1

* More often associated with fluid of some other gross appearance.

TABLE II

Diagnoses associated with 56 fluids of various gross appearances

Diagnosis	Purulent	Green	Other (Tan, brown, straw, amber, milky, etc.)
Perforation of duodenum or stomach		3	16 (5 of these were brown)
Acute pancreatitis (relatively mild)			3
Small bowel obstruction (without serious strangulation)			8
Peritonitis, secondary to:			
a. Acute appendicitis	6		2
b. Sigmoid diverticulitis		1	
c. Acute cholecystitis	1		
d. Mesenteric thrombosis	1 (Bloody pus)		
e. Rectal ulceration			1
Intra-abdominal abscess	2		
Acute appendicitis (without perforation)	2 (Probably *milky*)		1
Acute cholecystitis		1	
Leak from small bowel anastomosis			1
Leak from gastrostomy		1	
Carcinomatosis, serositis (active rheumatic fever), and ascites			2 each

NOTE: No gross description was given for two other fluids.

kind of fluid could be contaminants due to the technic of tapping. The presence of many bacteria usually indicated some form of peritonitis.

Cultures. The peritoneal fluid cultures, although of importance, do not contribute materially to the use of the abdominal tap as an aid to diagnosis of acute abdominal disease since the decision regarding diagnosis and the need for operation usually must be made long before any culture reports are available.

TABLE III

Correlation of microscopic findings in peritoneal fluid with diagnoses

Diagnosis	Number of Pts.	No. with Smears	White blood cells (Polymorphonuclears unless otherwise stated)	Red blood cells	Bacteria
1. Peritonitis	11	8			
Secondary to:					
a. Appendicitis	8	8	4+	0–1+	2+ (gm.-neg. Rods)
b. Cholecystitis	2	2	3+	0–2+	0–1+ (gm.-pos. Cocci)
c. Perforated rectal ulcer	1	1	4+	1+	2+ (gm.-neg. Rods)
2. Acute appendicitis	3	2	3+	—	—
3. Intra-abdominal hemorrhage (Spleen, liver omentum, ect. pregnancy, etc.)	7	1	0–1+	4+	—
4. Carcinomatosis	3	3	1+–2+	0–4+	—
5. Infarcted bowel	7	5	0–1	3–4+	—
			2+ to 3+ (late)		1–2+ (late variety)
6. Small intestine obstruction with early circulatory embarrassment	8	5	0–2+	0–2+	—
7. Pancreatitis—acute hemorrhagic	1	1	3+	3+	0
mild (edematous)	3	3	3+	1–2+	0 (cocci and rods described in one)
8. Perforated peptic ulcer	20	14	2–3+	0–1+	0–1+ (cocci) (Occasional debris)
9. Serositis (acute rheumatic fever)	2	2	2+ (mostly lymphocytes)	—	—
10. Ascites	3	1	1+ mostly lympho.	0–1+	—
11. Bowel contents—large	2	2	—	—	2+ (much debris)
small	2	2	—	—	4+ (much debris)

KEY: —, usually absent; 0, none; 1+, few; 2+, moderate number; 3+, many; 4+, loaded.

Acidity. The pH, determined by the use of nitrazine paper in 38 specimens of fluid, was neutral or alkaline in all but 6. Each of the acid fluids was associated with a leak from the gastroinestinal tract, 4 from perforated peptic ulcers, 1 from a perforated rectal ulcer, and 1 from a leaking small bowel anastomosis. The perforated peptic ulcers with acid fluids were not sealed off and 3 of the 4 were of short duration. Others, however, of no longer duration and unsealed, had an alkaline fluid.

Recently we have measured the quantity of free and total acid in the fluid, just as is done in a gastric analysis. Such determinations in 8 patients with a perforated peptic ulcer revealed no free acid in any, but a significant quantity of total acid in all but 1 (average 21 units, range 4 to 40 units). Similarly, no free acid was found in 6 fluids from other sources (perforated rectal ulcer, mesenteric thrombosis, peritonitis, ascites and 2 strangulated hernias). But in these 6 fluids the quantity of total acid was considerably less (average 10 units, range 0 to 30 units).

Amylase. Amylase determinations were made on the serum or the peritoneal fluid in 31 patients. Of these, 11 had both the serum and the peritoneal fluid tested for amylase activity (table IV). A comparison of the results in these 11 patients is of interest. Three (2 with small bowel obstruction without gangrene and 1 with a leak from a small bowel anastomosis) had no increased amylase

TABLE IV

Comparison of amylase activity in peritoneal fluid and blood in eleven patients

Diagnosis	Concentration of Amylase as Compared with Normal Values in Blood Serum	
	Peritoneal Fluid	Blood Serum
Perforated peptic ulcer	×11.0	×2.2
Perforated peptic ulcer	×8.0	×1.1
Perforated peptic ulcer	×5.3	×2.0
Perforated peptic ulcer	×13.3	×2.7
Average of 4 patients	×9.4	×2.0
Mild acute pancreatitis	×11.2	×8.0
Mild acute pancreatitis	×3.8	×3.0
Mild acute pancreatitis	×4.4	×2.5
Average of 3 patients	×6.5	×4.5
Small bowel obstruction		
With gangrene	×11.3	×4.3
Without serious strangulation	×1.2	×1.8
Without serious strangulation	×0.1	×0.9
Leaking small bowel anastomosis	×0.3	×0.5

TABLE V

*Comparison of amylase activity in peritoneal fluid and blood serum in thirty-one patients**

Diagnosis	Concentration of Amylase as Compared with Normal Value in Blood Serum			
	Peritoneal Fluid		Serum	
	No. of Pts.	Average	No. of Pts.	Average
Perforated stomach or duodenum	7	×9.3	10	×1.9
Acute pancreatitis (mild)	3	×6.0	4	×4.0
Small bowel obstruction				
a. With gangrene	1	×11.3	1	×4.3
b. Without gangrene	4	×0.6	3	×1.4
Perforated rectal ulcer	1	×7.8	—	—
Leak small bowel anastomosis	1	×0.3	1	×0.5
Carcinomatosis	1	×0.5	—	—
Ascites	1	×0.4	—	—
Leak of gastrostomy	—	—	1	×1.2
Perforated appendix with peritonitis	—	—	1	×0.5
Acute cholecystitis	—	—	1	×0.5
Acute cholecystitis, perforated	—	—	1	×0.4

* These 31 patients include the 11 patients in whom both the peritoneal fluid and blood serum amylase determinations were made (table IV), 8 patients with only peritoneal fluid determination, and 12 patients with only blood serum determinations of amylase activity.

activity in either the fluid or serum. The 4 patients who had a perforated peptic ulcer had a much higher amylase activity in the peritoneal fluid than in the serum (9.4:2.0). In the 3 patients with mild acute pancreatitis, the findings were similar but the difference between the fluid and the blood amylase was less marked (6.5:4.5). The other patient in this group, with a gangrenous small bowel obstruction, also had a higher amylase content in the peritoneal fluid than in the serum (11.3:4.3).

The amylase content was very low in the peritoneal fluids of carcinomatosis, ascites and small bowel obstruction without gangrene, but was markedly elevated in those of perforated peptic ulcer and pancreatitis (table V).

False positive taps. In 2 instances, fluid was obtained by paracentesis when no free fluid existed intraperitoneally. In 1, gross blood was obtained after the needle was inserted well below the abdominal muscle layers. At exploration, the patient was found to have a ruptured left inferior epigastric artery which had bled extraperitoneally, pushing the anterior parietal peritoneum posteriorly a distance of about 2 inches. The point of the needle had remained in the extraperitoneal hematoma. The second *false positive* tap was in a one week postoperative patient who had a large, left, polycystic kidney. A cyst of the kidney was entered by the needle and serous fluid returned. Reoperation because of wound dehiscence revealed no free abdominal fluid.

A condensed summary of the fluid characteristics usually found with the various causes of peritoneal fluid is given in table VI.

TABLE VI

Summary of usual characteristics of fluid associated with various diagnoses

Diagnosis	No. of Cases	Gross Appearance	pH	Smears			Amylase
				White blood cells	Red blood cells	Bacteria	
Intra-abdominal hemorrhage (rupture of solid organ, ectopic preg., etc.)	7	Whole blood	Alk.	0–1+	4+ (norm. blood smear)	0	
Intestinal obstr. with infarction of bowel	7	Bloody to serosanguineous	Alk.	1–2+ (more if late)	3–4+	0 (1–2+ if late)	11.3× normal blood content (serum amylase less elevated)
Without serious strangulation	8	Straw-colored	Alk.	0–2+	0–2+	0	Not elevated
Perf. of duodenum or stomach	20	Cloudy, yellow or brown, occ. green	Alk. (occ. acid)	2–3+	0–1+	0–1+	9.3× normal blood content (serum amylase only slightly above normal)
Pancreatitis, acute (relatively mild)	4	Cloudy yellow to reddish brown	Alk.	3+	1–3+	0	6.3× normal blood content (serum amylase elevated less)
Peritonitis, secondary to:							
a. Acute appendicitis with perf.	8	Purulent fecal odor	Alk.	4+	0–1+	2+ (Gram neg. rods)	
b. Acute cholecystitis with perf.	2	Purulent	Alk.	3+	0–2+	0–1+	
c. Mesenteric throm. (late)	1	Bloody, purulent	Alk.	3+	3–4+		
Intra-abdominal abscess	2	Purulent	Alk.	4+	0	2+	
Acute appendicitis	3	*Milky*	Alk.	3+	0	0	
Serositis (active rheum. fever)	2	Serous	Alk.	2+ (mostly lympho)	0	0	
Ascites	3	Serous, sl. turbid	Alk.	2+ (mostly lympho)	0–1+	0	Not elevated
Carcinomatosis	3	Serous to bloody	Alk.	1–2+	0–4+	0	Not elevated

DISCUSSION

The data used in this study were accumulated largely through the combined efforts of the members of the surgical house staff of the Salt Lake General Hospital. The fact that the house staff was sufficiently interested in the procedure to use it often and to record the data faithfully is, in itself, a real tribute to the value of the procedure. Its value has been proved so often that it now is routine on our surgical wards when the diagnosis of an acute abdominal disease is in doubt.

Occasionally *an error in interpretation* may be made. Our worst error was in a 40 year old alcoholic addict who was known, from previous admissions, to have recurring bouts of acute pancreatitis. He was admitted Jan. 9, 1953 with severe pain in his left upper abdominal quadrant, similar to his previous episodes. The vital signs were moderately increased and his abdomen was diffusely tender and moderately rigid. Rebound tenderness was referred to the left para-umbilical area. Peritoneal tap revealed a reddish-brown fluid, with a mild fecal odor, containing numerous white blood cells, red blood cells and gram-negative bacilli. The fluid pH was 8.0, and no free or total acid was detectable. The amylase activity of the peritoneal fluid was 11.3 times the normal blood content and of the blood was 4.3 times the normal blood content. These fluid findings were different from any previously encountered. We mistakenly decided that he had acute pancreatitis and treated him conservatively. He failed to respond and died 26 hours after admission. Autopsy revealed a strangulated, gangrenous, internal hernia of the jejunum, with, a purulent peritonitis. The fecal odor, and the E. Coli probably should have informed us that pancreatitis was unlikely. Too much faith was placed in the increased amylase. Such errors have been rare in the past and will become more rare in the future as more information is gathered concerning the meaning of the various fluid characteristics.

Some of the generalities which follow are tentative, but they have become useful in interpreting the results of diagnostic taps.

The negative tap. A *negative tap* means that no peritoneal fluid was obtained, but does not necessarily mean that no free peritoneal fluid exists. Of the 91 taps made, 24 yielded no fluid for study. Sixteen of the 24 negative taps proved to be *true negative* taps and 8 were *false negatives*. Fewer *false negatives* have been obtained since beginning the routine of emptying the needle onto a slide for examination when no fluid entered the syringe. The routine use of a needle with a stylet in place during its insertion probably will further decrease this fault. A negative tap has relatively little significance. If, clinically, exploration is clearly indicated, a negative tap should never prevent operation. When the need for operation is less clear, a negative tap may be considered as slight evidence in favor of further observation. A negative tap is reassuring in those instances in which we are already inclined not to operate. Similar interpretations of a negative tap have been advised by Neuhof and Cohen,[9] and Denzer.[4]

Bloody fluid. In a few instances only a few drops of blood were obtained by tap. These are referred to as *bloody taps* and usually mean that a vessel was encountered by the needle as it punctured the abdominal wall. Such a tap has *no*

diagnostic significance, since a free flow of blood usually is obtained if there is an appreciable quantity of blood in the peritoneal cavity.

The finding of grossly bloody fluid within the peritoneal cavity, with few exceptions, indicates the need for operation. The main exceptions are acute hemorrhagic pancreatitis and carcinomatosis. It has been stated that ascites from cirrhosis of the liver or heart failure occasionally may be grossly bloody, but we have not observed this. With a history of trauma, bloody fluid indicates intra-abdominal bleeding and the need for operation. The importance of bloody peritoneal fluid in a patient who has had trauma to the abdomen was illustrated by a 13 year old boy who had been hit by a truck. There was a fracture of the left clavicle with contusion of the left side of his chest. Abdominal pain and physical signs were minimal. His state of shock was thought to be due to the contusions and pain with a large neurogenic factor. The finding of whole blood in the left lower quadrant of his abdomen by peritoneal tap made the diagnosis of ruptured spleen. Subsequently, transfusions and splenectomy saved this boy's life. This type of fluid in a young woman suggests the possibility of a ruptured ectopic pregnancy. Recently, a 25 year old Negro woman was seen here by a gynecologist for obscure abdominal pain. Her history and physical findings were such that acute appendicitis was suspected. She was referred to a general surgeon, who found grossly bloody fluid by peritoneal tap and returned the patient to the gynecologist for operation. A ruptured tubal pregnancy was found. With a known intra-abdominal carcinoma, bloody fluid by tap may indicate the hopelessness of the situation and justify nonoperative therapy.

In *small bowel obstruction*, the presence of bloody peritoneal fluid is of great importance. Hill and associates[5] produced strangulation obstruction in the small intestine of 4 dogs and found that *rusty* fluid, containing many red blood cells, invariably was present within four hours. In 2 of the dogs only white blood cells were seen in the clear fluid obtained by tap at one and two hours. Crowley and Winifield,[3] in reviewing the problems of internal strangulating obstruction, emphasize the difficulties in diagnosis. They point out that, sooner or later, extravasation of blood occurs into the peritoneal cavity in practically all cases of strangulating obstruction. To them, bloody fluid obtained by paracentesis provides one of the most indicative signs in the differentiation of simple from strangulating obstruction lesions.

Our experience with small bowel obstruction is in agreement with these observations. Early in a strangulating obstruction, the peritoneal fluid is straw-colored and contains a fair number of polymorphonuclear cells, few or no red blood cells, and no bacteria. In our experience, a frankly bloody fluid in such patients invariably indicates a serious strangulation, usually with nonviable bowel which must be resected. If seen even later, infection is superimposed, producing a bloody purulent fluid.

Purulent fluid. The presence of pus, free in the peritoneal cavity, indicates peritonitis. Most, with the exception of primary peritonitis, are just as well, if not better, treated by operation. But operation is contraindicated in primary peritonitis since there is no local, intra-abdominal focus of infection to be corrected. Neuhof and Cohen,[9] Denzer,[4] Campbell,[1] and Steinberg[11, 12] have em-

phasized the importance of studying a smear of the peritoneal fluid in differentiating a primary peritonitis, due to pneumococci, streptococci or gonococci, from a secondary peritonitis, as occurs after rupture of an acutely inflamed appendix. They state that the presence of gram-positive diplococci (with an occasionally demonstrable capsule) or cocci predominantly in chains, or gram-negative, kidney-shaped diplococci, predominantly intracellular, are characteristic of pneumococcic, streptococcic and gonococcic peritonitis, respectively. Particularly when one of these findings occurs in a child with a vaginal discharge containing similar organisms, or with a severe sore throat, or with pneumonia, one should assume that the peritonitis is a primary type and elect to observe rather than to operate. The absence of large numbers of bacteria in the smear is much against a primary peritonitis.

Neuhof and Cohen[9] found a tap helpful in 10 children with pneumococcic peritonitis and in several cases of streptococcic peritonitis. In their study of over 200 patients with appendicitis, a pure culture of streptococci was found only twice.

The presence of many gram-negative rods, with or without a few cocci, with many polymorphonuclear cells usually means that the peritonitis is secondary to a perforation of the appendix or some portion of the large bowel. A fecal odor is common. Late cases of strangulated obstruction show many red blood cells in addition to polymorphonuclear cells, with or without bacteria. Peritonitis following perforation of a gallbladder may show no bacteria on smear, but the presence of E. Coli, or cocci is compatible.

Steinberg[12] has studied extensively smears of peritoneal fluids and uses them not only for diagnosis but also for determining the prognosis in patients with peritonitis. The number of free bacteria on the smear seems to be the important factor in determining prognosis. We have not attempted to study the fluids from this viewpoint.

Other types of fluid. The gross appearance of fluids which were neither bloody nor purulent was less helpful. In some of the leaks from the upper gastrointestinal tract or the gallbladder, the fluid was green. A *milky* fluid, containing many polymorphonuclear cells, but no bacteria, is common with an unruptured, acute appendicitis. However, many of the causes of the *acute abdomen* early may exhibit a light colored, straw, amber, tan, brown, serous or cloudy fluid. Particularly with these types of fluid, further tests, especially a microscopic examination of the smear and an amylase determination, are of great value.

Microscopic examination may help as in differentiating the abdominal pain of serositis associated with active rheumatic fever from acute appendicitis. No bacteria and many white blood cells are seen in both conditions, but, whereas polymorphonuclear cells prdominate in acute appendicitis, lymphocytes are most common with serositis. Recently a 9 year old girl was seen who illustrated this quite well. She complained of epigastric pain which became generalized. She had been anorexic and nauseated, but had not vomited. Tenderness with some guarding was present, chiefly just to the the right of the umbilicus. There was a leukocytosis of 16,000. A previous history of acute rheumatic fever with migrating polyarthritis suggested that this pain might be due to an associated

serositis. Peritoneal tap revealed two drops of *milky* fluid, containing many lymphocytes, only an occasional polymorphonuclear cell, and no bacteria. A nonoperative course was chosen, chiefly on the strength of the peritoneal fluid findings. Her subsequent course has indicated that the choice was wise.

In the further study of such fluids, the *amylase* measurements have proved to be of considerable value, particularly in regard to patients with pancreatitis or perforated peptic ulcer. Keith, Zollinger and McCleary[7] compared the amylase activity of the blood with that of the peritoneal fluid in 12 patients with acute pancreatitis. The amylase content of the peritoneal fluid was consistently higher than of the blood in each patient. In most, the fluid amylase values were sustained at a diagnostic level two to four days longer than the relatively transient blood amylase. In 6 of the 8 patients listed by Howard[6] the peritoneal fluid amylase level was markedly elevated. Pemberton and others[10] found a high concentration of amylase in the peritoneal fluid of 4 dogs in which perforation had been created in the duodenum anteriorly. The serum amylase in these animals was only moderately elevated.

Our findings regarding the amylase of the peritoneal fluid in perforated peptic ulcers and in pancreatitis, although not statistically significant, support these reports. The difference between the amylase levels of the blood and peritoneal fluid was greater in patients with perforated peptic ulcer than in those with pancreatitis. The peritoneal fluid content was consistently higher than the blood levels in each condition. Also of interest was the elevated amylase level in both fluid and blood with bowel strangulation.

The acidity of the peritoneal fluid has been of less value than anticipated. We had hoped that the acid entering the peritoneal cavity from a perforated ulcer commonly would give the fluid an acid reaction and thus differentiate a perforated ulcer from most other intra-abdominal catastrophies. However, in only 4 of 20 patients with perforations of the stomach or duodenum was the fluid acid by nitrazine paper.

Experimentally[8] we have found that N/20 hydrochloric acid, which has a pH of 2.2 and contains 50 units of free HCl per 100 cc., injected into the peritoneal cavity of the dog, changes very rapidly. The free acid regularly disappears within 35 minutes after being injected and combined acid is detectable in the peritoneal fluid in significant quantities within 5 minutes. The combined acid reaches an early peak of 12 units at 35 minutes; gradually increases to 18 to 20 units at 12 hours; and slowly declines thereafter to an average of 10 units at 24 hours after injection. The quantities of free and total acid in the peritoneal fluids of patients are of no diagnostic importance at present. Fluid with an acid reaction favors the diagnosis of an unsealed perforated peptic ulcer, but an alkaline fluid more commonly is found in this situation.

The meaning of some of the fluid characteristics are not yet clear. Many of the examinations in this study were made for our enlightenment concerning the significance of certain properties of the fluid, and are unnecessary in the practical application of peritoneal taps as an aid to diagnosis. The gross appearance alone frequently is informative enough to indicate the need for operation without further examination of the fluid. A simple unstained smear, likewise, often reveals

the needed information. Occasionally, further tests reveal the true nature of the disease, but they need not be routinely done.

SUMMARY AND CONCLUSIONS

In our opinion, the diagnostic peritoneal tap is a safe and valuable aid in diagnosis of acute abdominal disease. Its value and safety, together with its simplicity, warrant its general acceptance and frequent use.

The diagnostic peritoneal tap, although it yields very valuable information, is still a much neglected aid in differential diagnosis of the acute condition within the abdomen. Fear, the main reason for its lack of general acceptance, is unwarranted, since the needle rarely enters the bowel, and, when it does, no significant leakage occurs. These conclusions are based on laboratory and clinical experience.

The technic and precautions to be observed are presented. No significant complication occurred in an experience of 91 peritoneal taps.

The peritoneal fluids of 75 patients were studied. The gross appearance, microscopic findings, pH, and amylase content of the fluids are analyzed and correlated with the causes of free peritoneal fluid.

Of particular interest was the high amylase content of the peritoneal fluids associated with pancreatitis and with perforated peptic ulcers.

A negative tap is of little diagnostic significance.

Examples are cited in which a peritoneal tap was invaluable.

The practicality of this procedure is evidenced by the frequency with which our surgical house staff voluntarily uses it.

The diagnostic peritoneal tap should be a generally accepted and frequently used aid in the differential diagnosis of the acute condition within the abdomen.

REFERENCES

1. Campbell, H. E.: Abdominal puncture; practical aid in diagnosis, Rocky Mountain. M. J. *43:* 305 (April) 1946.
2. Coller, F. A., and Brinkman, H.: Studies on reaction of peritoneum to trauma and infection. Ann. Surg. *109:* 942 (June) 1939.
3. Crowley, R. T., and Winfield, J. M.: Collective review; internal strangulating obstruction of bowel, Internat. Abstr. Surg. *89:* 417 (Nov.) 1949, in Surg., Gynec. & Obst. (Nov.) 1949.
4. Denzer, B. S.: Abdominal puncture in diagnosis of peritonitis in childhood, J. Pediat. *8:* 741 (June) 1936.
5. Hill, F. C.; O'Loughlin, B. J., and Stoner, M.: Peritoneal aspiration in diagnosis of strangulated bowel, Surg., Gynec. & Obst. *74:* 121 (Jan.) 1942.
6. Howard, J. M.: Symposium on recent advances in surgical physiology; surgical physiology of pancreatitis, S. Clin. North America *29:* 1789 (Dec.) 1949.
7. Keith, L. M., Jr.; Zollinger, R. M., and McCleery, R. S.: Peritoneal fluid amylase determinations as aid in diagnosis of acute pancreatitis, Arch. Surg. *61:* 930 (Nov.) 1950.
8. Moretz, W. H., and Erickson, W. G.: Fate of free hydrochloric acid in peritoneal cavity of dog. To be published.
9. Neuhof, H., and Cohen, I.: Abdominal puncture in diagnosis of acute intraperitoneal disease, Ann. Surg. *83:* 454 (April) 1926.
10. Pemberton, A. H.; Grindlay, J. H., and Bollman, J. L.: Serum amylase levels after acute perforations of duodenum: preliminary report, Proc. Staff Meet., Mayo Clin. *25:* 5 (Jan. 4) 1950.
11. Steinberg, B.: Stages in peritonitis based on defense mechanism in relation to treatment, Arch. Surg. *39:* 770 (Nov.) 1939.
12. Steinberg, B.: Peritoneal exudate; guide for diagnosis and prognosis of peritoneal conditions, J.A.M.A. *116:* 572 (Feb. 15) 1941.
13. Steinberg, B., and Martin, R. A.: Diffusion and localization of experimental infections of peritoneum, Surg., Gynec. & Obst. *79:* 457 (Nov.) 1944.
14. Wangensteen, O. W.: Intestinal Obstructions, ed. 2, Springfield, Ill., Charles C Thomas, 1942.

SARCOMA OF THE UTERUS. A STUDY OF NINETEEN PATIENTS

PAUL D. BRUNS, M.D.
BRUCE M. PORTER, M.D.
R. M. MULLIGAN, M.D.

Denver, Colo.

INTRODUCTION

Late diagnosis and inadequate treatment remain important factors in the persistently high mortality rate from sarcoma of the uterus, even though the degree of malignancy and hematogeneous spread of the various sarcomas to be discussed are admittedly great. The purpose of this review is to emphasize an additional procedure which may increase the number of early diagnoses thereby enhancing the salvage rate of uterine sarcoma.

Between July 1944, and June 1953, 16 cases of uterine sarcomas were studied at the Colorado General Hospital and the Denver General Hospital. Three cases were obtained from the files of three private physicians in Denver. Nine other cases were excluded from the study; 3 undifferentiated endometrial carcinomas, 2 leiomyomas with sarcomatoid reaction, 1 benign cellular leiomyoma, 1 stromal endometriosis, 1 adenomyosis, and 1 probable malignant melanoma.

The youngest patient in this study was 30 years old, the oldest 75 years with an average of 50 years. Two-thirds of the patients were postmenopausal. Eleven patients were diagnosed and treated initially, 6 had previous incomplete pelvic operations, and 2 had been given pelvic irradiation. The chief presenting symptoms were vaginal bleeding, discharge, pain, and weight loss. A lower abdominal mass could be outlined in all instances. Neoplastic tissue protruded from the cervix in 5 patients. Vaginal smears done at the time of admission to the hospital were positive in 5 patients, suspicious in 2, negative in 1, and not obtained in the remaining patients. The following 17 cases of sarcoma were studied: leiomyosarcoma 7, endometrial sarcoma 4, rhabdomyosarcoma 4, liposarcoma 1, and unclassified 1. The other 2 cases were a mixed mesodermal tumor and a malignant mesenchymoma.

LEIOMYOSARCOMA

The prevailing opinion is that most leiomyosarcomas originate within a preexisting leiomyoma by malignant change of its smooth muscle. Analysis of the 7 patients with leiomyosarcoma showed the following; (a) previous incomplete pelvic surgery (partial hysterectomy, myomectomy, polypectomy); (b) previous pelvic irradiation; (c) symptoms of fibroids (menometrorrhagia, tumor and pain);

From the Department of Obstetrics and Gynecology and the Department of Pathology, University of Colorado School of Medicine, Colorado General Hospital and Denver General Hospital, Denver, Colorado.

A portion of this material appeared in an unpublished thesis submitted to the Faculty of the Graduate School of Medicine, University of Colcrado, in partial fulfillment of the requirements for the Degree of Master of Science in Obstetrics and Gynecology by Bruce M. Porter, M,D., present address; 1325 Hickory Street, Abelene, Texas.

(d) no preoperative diagnosis; and (e) diversified types of therapy. One patient died from intestinal obstruction. Two died presumably from peritoneal and pulmonary metastases. The remaining 4 were alive and without disease at their last visit.

On microscopic examination, the tumor cells were relatively uniform and spindle shaped. The nuclei were oblong or ovoid and contained abundant, heavily stippled chromatin. Mitoses were numerous and giant cells were scarce. Longitudinal myofibrils could be seen with the Gomori trichrome stain. Wilder reticulum stain showed the pattern characteristic of smooth muscle tumor.

From a clinical point of view, complete hysterectomy and adnexectomy offered the best prognosis, provided the tumor was discovered and treated at an

TABLE I

Leiomyosarcoma of the uterus

History	Findings	Treatment	Follow-up
No. 1 30 yr. 1944 Discharge 5 mo.	Fibroids *Leiomyosarcoma*	Myomectomy and roentgen ray therapy	Well, no recurrence 10–1–46 No follow-up
No. 2 34 yr. 1950 Pelvic operations in 1949 & 1950	Pelvic mass *Leiomyosarcoma*	Palliative roentgen ray therapy	Died from sarcoma 10–4–50
No. 3 39 yr. 1948 Discharge 6 wk. Bleeding 6 wk.	"Recurrent polyps" *Leiomyosarcoma*	Total hysterectomy Bilateral salpingectomy & oophorectomy	Well, no recurrence 1–14–52 No follow-up
No. 4 41 yr. 1953 Menorrhagia 2 yr.	Fibroids *Leiomyosarcoma*	Total hysterectomy Bilateral salpingectomy & oophorectomy	Well, no recurrence 10–23–53
No. 5 54 yr. 1945 Bleeding 5 mo.	Cervical polyp Pelvic mass *Leiomyosarcoma*	Roentgen ray and radium therapy	Lung metastases 7–14–48 Presumably dead
No. 6 57 yr. 1949 Bleeding 6 mo.	Necrotic Curettings *Leiomyosarcoma* Pap. smear III	Radium followed by total hysterectomy Bilateral salpingectomy & oophorectomy	Well, no recurrence 1–7–53
No. 7 71 yr. 1951 Pelvic roentgen ray therapy 1932	Fibroids *Leiomyosarcoma*	Excision metastatic tumor tissue	Ascites 7–17–51 Presumably dead

early stage. Early discovery may be possible in cases of leiomyosarcoma which break through the endometrium and shed neoplastic cells by routine cytologic screening (table I).

ENDOMETRIAL SARCOMA

Analysis of the patients with endometrial sarcoma demonstrates that an early diagnosis is seldom made and that a majority of patients already have distant metastases when first seen. Once an endometrial sarcoma has progressed to the point of vaginal bleeding, the usual presenting symptom, the lesion is seldom amenable to palliation or cure. One patient had smears taken from the vagina and cervix at the time of admission to the hospital. These were positive. This suggests that widespread cytologic screening may offer the best hope of early diagnosis.

One of the 4 patients with endometrial sarcoma had received intrauterine radium four years previously. All patients in this series exhibited vaginal bleeding from three months to one year prior to treatment. The gross pathologic lesion was usually a polypoid mass of tissue in the fundus of the uterus.

Microscopically, the cells were short, spindle, polyhedral or round, sometimes stellate and surrounded by mucoid stroma. The nuclei were enlarged, hyperchromatic and frequently showed bizarre mitoses. Noncancerous or atrophic endometrial glands were observed in each patient (table II).

RHABDOMYOSARCOMA

The most striking clinical observation about these 4 patients was the 100 per cent mortality rate. These tumors usually grew rapidly and metastasized early.

TABLE II

Endometrial sarcoma

History	Findings	Treatment	Follow-up
No. 8 48 yr. 1945 Bleeding 1 yr.	Red-grey tissue *Endometrial sarcoma*	Palliative roentgen ray therapy	Metastases Died from sarcoma 7/16/45
No. 9 51 yr. 1949 Radium 1945 Bleeding 6 mo.	Polypoid tissue *Endometrial sarcoma*	Total hysterectomy Bilateral salpingectomy & oophorectomy	Well, no recurrence 10/23/53
No. 10 69 yr. 1951 Pelvic op. 1950 Bleeding 1 yr.	Grey tissue *Endometrial sarcoma*	None	Metastases Died from sarcoma 2/5/51
No. 11 75 yr. 1953 Bleeding 6 mo.	Polypoid tissue *Endometrial sarcoma* *Pap. smear IV*	Total hysterectomy Bilateral salpingectomy & oophorectomy	Metastases Died from sarcoma 8/26/53

The longest survival was one year after the first admission. Strangely enough, this tumor regressed dramatically with roentgen irradiation and probably prolonged the life of the patient for at least one year. Grossly, all the tumors appeared in the uterus or upper vagina and cervix as polypoid friable growths. Two could have been classified as *sarcoma botryoides*. Vaginal smears were positive in 2 cases again suggesting the value of this procedure as a screening test. As usual, the type of treatment was not decisive because blood and/or lymphatic spread had already occurred before definitive therapy was begun. The value of a preoperative chest roentgenogram and the hazards of vaginal and pelvic operative procedures in advanced rhabdomyosarcoma were demonstrated by these 4 patients. Microscopic study of many blocks of these four tumors by hematoxylin and eosin and Gomori trichrome stains revealed cellular pleomorphism as indicated by spindle, polyhedral, and giant tumor cells, nuclear hyperchromatism and multiplicity, huge irregular pleuripolar mitoses, and both longitudinal and cross striations in all 4 cases (table III).

MESODERMAL TUMOR OF THE UTERUS

A recent review of this rare uterine tumor gives 150 reported cases. Most reviews and case reports repeatedly emphasize the *confusing and controversial* nature of this tumor. Some even intimate that it may represent an iatrogenic disease occasioned by the physician who treats a patient with pelvic irradiation for a benign condition.

TABLE III

Rhabdomyosarcoma of the uterus

History	Findings	Treatment	Follow-up
No. 12 48 yr. 1950 Abd. mass 3 yr. Bleeding 7 mo.	"Prolapsed fibroid" *Rhabdomyosarcoma* *Pap. smear IV*	Total hysterectomy Bilateral salpingectomy & oophorectomy	Died from sarcoma 2/24/50
No. 13 48 yr. 1951 Pelvic op. 1950 Weight loss 6 mo.	"Pelvic mass" *Rhabdomyosarcoma*	Radium	Died from sarcoma 1/11/52
No. 14 52 yr. 1952 Discharge 6 wk. Bleeding 2 wk.	"Vaginal grapes" *Rhabdomyosarcoma*	Wertheim hysterectomy	Died from sarcoma 2/10/53
No. 15 68 yr. 1952 Pelvic op. 1949 Bleeding 3 yr.	"Vaginal grapes" *Rhabdomyosarcoma* *Pap. smear IV*	Roentgen ray therapy	Died from sarcoma 10/5/53

CASE REPORTS

Case 1. The patient, no. 16, with a malignant mesenchymoma was a 52 year old white woman, para 0, who was first seen March 30, 1953. Her menarche occurred at the age of 16; the menses was irregular and was accompanied by menorrhagia and dysmenorrhea. The climacteric occurred in 1951. Her past history was characterized by recurrent episodes of peptic ulcer hematemesis and urinary tract infections. Her present illness began three weeks prior to admission with vaginal spotting, dysuria, and partial urinary retention.

On examination, the vital signs were normal with the exception of a blood pressure of 200/120. An irregular firm pelvic mass extended halfway to the umbilicus. A small quantity of blood was present in the cervix. A vaginal smear was IV positive and the endometrial biopsy showed malignant mesenchymoma. On March 13, 1953, a total abdominal hysterectomy and bilateral salpingo-oophorectomy was done without postoperative complications. The entire specimen weighed 900 Gm. Multiple polypoid masses were attached to the endometrium. The left side of the uterus contained a small mass.

The microscopic sections showed malignant rhabdomyoblasts in all stages of development. Cross striations were identified in the tumor cells. Malignant lipoblasts, malignant mesenchymal cells, and mature cartilage were also identified. Since no cancerous epithelial cells were found in many sections, the diagnosis of malignant mesenchymoma was made.

Two months after operation the patient was well with no apparent recurrence. Vaginal smear was again of aid in diagnosis.

Case 2. Patient, no. 17, was a 58 year old white woman, para 1, admitted to the hospital in December 1952, because of vaginal bleeding for several months. Material from a curettage was diagnosed as adenocarcinoma and the patient was treated with intracavitary radium. Six weeks later a total hysterectomy was done. The gross specimen showed a polypoid grey mass in the fundus. On microscopic examination both carcinomatous and rhabdomyosarcomatous elements were found in this endometrial polyp.

In June 1953, a laparotomy, done because of a rapidly enlarging abdomen, showed massive peritoneal metastases. Histologic study of the tumor demonstrated both carcinoma and sarcoma with the latter the predominant element. The patient died in August 1953; no autopsy was obtained. The final diagnosis was mixed mesodermal tumor of the uterus.

OTHER TUMORS OF THE UTERUS

Case 1. The patient, no. 18, was 58 years of age when admitted to the hospital on Aug. 18, 1952. She had her menopause in 1941. Her present symptoms began one month prior to admission with uterine cramps, pain, and the passage of tissue, said to have been *malignant*. Upon examination, the uterus was symetrically enlarged to twice normal size. Vaginal smears were reported as *suspicious* and the preoperative diagnosis of adenocarcinoma was made. Curettage revealed sarcoma of the uterus. August 21, a total abdominal hysterectomy with bilateral salpingo-oophorectomy was completed without postoperative complications. The specimen weighed 118 Gm. On the anterior wall of the fundus of the uterus was a red-brown, soft, polypoid mass projecting into the lumen.

Microscopic examination, with hematoxylin and eosin stain, showed sheets and bands of cells with hyperchromatic nuclei and basophilic cytoplasm. Pleomorphic polyhedral giant cells were present in a mucoid matrix containing many small anastomosed blood vessels. The Gomori trichrome stain showed green cytoplasm and no longitudinal or cross striations in the cells. The Sudan IV stain showed many fine to medium fat globules in the tumor cells in well preserved areas.

The diagnosis of liposarcoma was made with considerable reluctance and after careful consideration. The only other alternative was to list this case as an unclassified sarcoma. Only 1 previous case of liposarcoma has been mentioned in the literature.

Case 2. The patient, no. 19, was a 74 year old woman who was admitted to the hospital in June 1950. She gave the history of progressive weight loss for one year and vaginal bleeding for three months. On examination the pelvis and lower abdomen were filled with a firm

mass. Uterine tissue removed for biopsy was studied by differential stains in multiple areas. A final diagnosis of sarcoma of the uterus was made, type unclassified. The patient died shortly after admission to the hospital and no autopsy was obtained.

DISCUSSION

Use of the vaginal smear in this series, although used late in the course of the disease, was of diagnostic value in 7 patients. Five different types of uterine sarcoma were reported by smear either as suspicious (III) or positive (IV). The differentiation of sarcoma from carcinoma by the smear technic is seldom possible. To the experienced observer, some cells suggest sarcoma. Cells with the same general characteristics appear in smears from patients with undifferentiated squamous cell carcinoma of the cervix. Differential diagnosis is further hampered because urinary tract sarcomas may also shed cells carried by the urine into the vagina. The screening technic provides a high degree of *early suspicion* which is necessary to *early diagnosis* by the more conventional methods.

SUMMARY AND CONCLUSIONS

Nineteen cases of uterine sarcoma included 7 leiomyosarcomas, 4 endometrial sarcomas, 4 rhabdomyosarcomas, and 1 malignant mesenchymoma, 1 mixed mesodermal tumor, 1 liposarcoma, and 1 unclassified sarcoma.

In 11 patients, diagnosis and treatment were primary; in 6, previous incomplete pelvic operations had been made; and in 2, previous pelvic roentgen-irradiation had been used for presumably benign conditions.

Abstracts of the histories of the patients with the malignant mesenchymoma, the mixed mesodermal tumor, and the liposarcoma have been presented.

Cytologic screening by vaginal, cervical and endometrial smears are recommended as an adjunct to early diagnosis of the types of uterine cancer presented.

ACKNOWLEDGMENT

Our gratitude is extended to Dr. Warren W. Tucker, Dr. Lyman W. Mason, and Dr. Eugene S. Auer for permission to use their cases in this survey. We wish to acknowledge our appreciation to Dr. Karl T. Neubuerger, Dr. Alexis E. Lubchenco, Dr. S. M. Prather Ashe, Dr. Walter T. Wikle and Dr. Emeric I. Dobos for making the pathologic material available for study.

THE USE OF FEMORAL HEAD PROSTHESES IN FRACTURES

WILLIAM F. STANEK, JR., M.D., JAMES S. MILES, M.D., LYNN O. KEYS, M.D. AND HOWARD D. GRAHAM, M.D.

Denver, Colo.

In the transition period of a new operation between original experimental use and general acceptance many problems arise, the answers to which are not found in the first articles written about the procedure. The operation of femoral head replacement is no exception. In the available journals the individual articles deal with a particular prosthesis developed by the author, advocating the use of his prosthesis, and almost without exception show good results with few complications[1, 2, 3, 6, 7]. The only general report on the subject is the "Preliminary Survey of Femoral Head Prostheses" of the American Academy of Orthopedic Surgeons.[4] Since this article lists 37 different prostheses, and the advertising section of the same issue of the Journal of Bone and Joint Surgery illustrates 13 types, it is understandable that the orthopedic surgeon undertaking his first case will have some difficulty in choosing a prosthesis. Adding to this problem is the cost of the prosthesis, the various sizes needed and the lack of local availability of many of these replacements.

It is our belief that standardization of the procedure of femoral head replacement can result only from the reporting of many independent series of cases. To be of value the results of a particular procedure must be as successful in the hands of competent surgeons as it is in the reports of the originator. Complications must not be excessive, and in the case of a failure of the procedure, all hope of rehabilitation should not be destroyed.

In undertaking the use of the femoral head prosthesis, the orthopedic staff of the University of Colorado hospitals was not conducting an experiment either as to type of case suitable for the use of a prosthesis or as to type of prosthesis. The prostheses chosen were those most commonly advocated by recent authors, and the cases were those in which there was little question as to the advisability of their use. The cases reviewed were the first patients operated upon in the University Hospitals. They represent also the first experience of several of the surgeons with this procedure, and the difficulties recorded may, in part, be due to this.

Since no experimental consideration influenced the decision to insert a femoral head prosthesis, the following were the indications for its use:

A. To overcome the failures of previous therapy:
   1. In nonunion of a femoral neck fracture.
   2. In aseptic necrosis of the femoral head. (In these instances replacement must offer a greater margin of success and, preferably, a simpler procedure than other reconstructive methods.)

From the Department of Surgery, Division of Orthopedic Surgery, University of Colorado School of Medicine, Denver, Colorado.

B. To shorten hospitalization, lessen morbidity and eliminate the necessity for further surgery.
   1. In subcapital femoral fractures where nonunion is anticipated. (Particularly in the elderly patient where failure of routine nailing could not be followed by any secondary procedure.)

The prostheses available may be divided into types as follows:

A. Dependent upon the proximal surface of the femoral neck and the lateral intertrochanteric cortex for support—the original Judet.
B. Having a cuff extending beyond the artificial head to gain support from the neck in addition to the lateral intertrochanteric cortex—the modified Judet.
C. Inserting into the entire circumference of the neck and protruding through the lateral cortex—the *light-bulb* prosthesis of Thomson.
D. Using neck support plus a plate down the outer aspect of the femoral shaft—the Collison type.
E. Using neck support and a shaft extending down the medullary canal of the femur—the Moore or Thompson type.
F. Replacing the entire head, neck and trochanteric region of the femur—the McBride prosthesis.

McBride's discussion of the mechanical principles necessary in a prosthesis may well be repeated.[5]

1. Mechanical integrity of the prosthesis must be assured.
2. The method of anchorage must insure permanent stability.
3. Bone deterioration occurring in the course of time must not alter the stability of fixation.

Once these principles have been satisfied, simplicity of insertion and adaptability of the prosthesis to varying conditions of neck length and bone density become important.

The following tables illustrate the indications, methods, complications and results in this series (tables I to IV). All patients operated upon at Colorado General Hospital and Denver General Hospital—23 in number—have been reviewed. Nine were men and 14 were women. The age range was from 58 to 85 years with the average 73 years. Most patients were in poor physical condition since they came from lower income groups in the city. Excluded are the patients in whom a femoral head prosthesis was inserted for diseases other than traumatic, such as degenerative arthritis, rheumatoid arthritis and congenital dislocations with secondary degenerative changes. The patients with femoral neck and intertrochanteric fractures formed a group with similar criteria for evaluation. Fifteen different surgeons performed the operations reviewed in this series.

In table I a primary procedure designates one following a recent fracture in which the prosthesis was the original treatment. A delayed primary represents operation upon an untreated fracture of unknown duration.

In the evaluation of results, major emphasis was placed upon pain and stability. Range of motion, gait and patient satisfaction were of less importance. Pain is the most disabling symptom. Loss of stability manifested itself in the

TABLE I

Indication for prosthesis correlated with the result

	Total	Good	Fair	Poor	Failure	Unevaluated
Femoral Neck						
Primary	4			1		3 (2 deaths)
Delayed primary	3			1	1	1 (death)
Secondary nail failure	4	1	2			1 (death)
Aseptic necrosis (with or without union)	11	1	6	3		1
Intertrochanteric						
Secondary (nonunion)	1					1

TABLE II

Type of prosthesis correlated with the result

	Total	Good	Fair	Poor	Failure	Unevaluated
Judet: Acrylic	5		1	2		2
Metallic	3	1	2			
Collison	2		1	1		
Intramedullary	13	1	4	2	1	5

TABLE III

Surgical approach correlated with the result

	Total	Good	Fair	Poor	Failure	Unevaluated
Anterior	15	2	4	4	1	4
Posterolateral	8		4	1		3

TABLE IV

Treatment of the Capsule correlated with the result

	Total	Good	Fair	Poor	Failure	Unevaluated
Closed	17	1	7	4		5
Not sutured	2			1		1
Excised	4	1	1		1	1

prolonged use of crutches or canes, or in a severe limp. The range of motion was surprisingly good in most of these patients.

A result was considered to be excellent if the patient had no pain; walked without assistance; and had resumed normal activity. A good result was one in which the patient experienced minimal pain not requiring medication and minimal loss of stability evidenced by the use of a cane out of doors and no assistance indoors. A result was considered fair if the patient required medication to relieve pain produced by activity; if the patient was free of pain at rest; and if loss

of stability necessitated the use of crutches or cane. A result was considered poor if the patient had more pain than any of the above; and if the loss of stability limited his activity greatly. A result was classed a failure if the prosthesis had to be removed.

This series is not large enough to permit evaluation of the result with regard to the surgical approach or the treatment of the capsule at the time of the operation. However, these statistics are presented in tables III and IV. It is interesting that excision of the capsule did not prevent pain in these patients.

The complications are tabulated next. In the 3 patients with post operative infections, only one was so severe as to require removal of the prosthesis. This patient was an elderly woman in whom the operation was done as a delayed primary procedure. The prosthesis used was one of the intramedullary type. The extremity was not immobilized following the operation. Two days following surgery, the prosthesis dislocated, and closed reduction was unsuccessful because the prosthesis rotated in the femoral shaft. Pressure necrosis of the skin appeared over the dislocated prosthesis, and it had to be removed. The other 2 patients had mild infections—one drains small amounts intermittently, and the second has healed.

The one example of dislocation of the prosthesis is presented in table V. In 2 patients in whom the intramedullary type of prosthesis was used, the insertion of the prosthesis produced fractures of the inferior portion of the femoral neck. In one instance this fracture resulted in settling of the prosthesis and shortening. In the other, the fracture which extended into the intertrochanteric area healed without complication. Two of the intramedullary prostheses were inserted in-

TABLE V

Complications

Infection	3 (2 mild)
Dislocation	1
Fracture of portion of neck	2
Technical error (intramedullary stem protruding through cortex)	2
Pulmonary embolus (nonfatal)	1
Mortality (operative)	2

TABLE VI

Summary of results

Excellent	0
Good (Slight residual pain)	2
Fair (Major limitation stability)	8
Poor (Major disability pain 2; stability 3)	5
Failure (Infection and dislocation)	1
Unevaluated	7
Death, 4 (2 operative)	
Too recent, 2	
Lost, 1	

correctly—the intramedullary portion of the prosthesis perforating the cortex of the intertrochanteric region and protruding into the thigh muscles. This complication produced few symptoms. Two patients died in the postoperative period—1 at 10 days and the other at 15 days. Both patients were markedly debilitated and were over 80 years of age. Two other patients have died since surgery—1 three months postoperatively in a convalescent home and the other two and a half months following surgery while on a vacation trip.

DISCUSSION

Functional evaluation does not adequately express the surgical success obtained in the individual cases. The mental and general physical condition of the patient places a ceiling on the improvement to be expected. In this group senility, general debility and prolonged nonuse of the extremity were common. This series is too small to permit evaluation of the prosthesis used, the surgical approach or the treatment of the capsule. Some impressions have been formed by the authors from the series, from the literature and from experience gained elsewhere. No advantage is seen in the use of acrylic over metal. The Collison prosthesis is difficult to insert; has a fixed angle, and weakening of the neck transmits all of the force to the screws. One of the authors has experienced breaking of the screws. The McBride prosthesis was not used because of its mechanical complexity. The metallic modified Judet prosthesis is satisfactory where neck length is adequate and the bone at the proximal end of the neck is firm. An intramedullary support permits greater range of application since it can be used with a short femoral neck. To date no femoral neck has proved too long to permit its use. Insertion of the stem insures a correct neck-shaft angle. However, insertion of the stem offers considerable difficulty in some cases. The greatest criticism of the intramedullary prosthesis has been that the reconstituted head-neck length has not been sufficiently great.

CONCLUSIONS

There were no excellent (pain free, stable gait) results recorded in this series of 23 patients.

Instability has been a major factor in permanent disability.

Pain has been present in every case to some degree.

No conclusion as to the ideal prosthesis or operative procedure has been reached.

REFERENCES

1. Buxton, St J. D., and Waugh, W.: Complications and difficulties of Judet arthroplasty. J. Bone & Joint Surg. *35-B:* 57 (Feb.) 1953.
2. Judet, J., and Judet, R.: Use of artificial femoral head for arthroplasty of hip joint. J. Bone & Joint Surg. *32-B:* 166 (May) 1950.
3. Judet, R., and Judet, J.: Technic and results with acrylic femoral head prosthesis. J Bone & Joint Surg. *34-B:* 173 (May) 1952.
4. Lambert, C. N., Chairman, Committee on Scientific Investigation of the American Academy of Orthopaedic Surgeons: Preliminary survey on femoral-head prostheses, J. Bone & Joint Surg. *35-A:* 489 (April) 1953.
5. McBride, E. D.: Femoral-head prosthesis for hip joint, J. Bone & Joint Surg. *34-A:* 989 (Oct.) 1952.
6. Moore, A. T., and Bohlman, H. R.: Metal hip joint, case report, J. Bone & Joint Surg. *25:* 688 (July) 1943.
7. Thomson, J. E. M.; Ferciot, C. F.; Bartels, W. W., and Webster, F. S.: "Light bulb" type of prosthesis for femoral head, Surg., Gynec. & Obst. *96:* 301 (March) 1953.

INSULIN INDUCED STRESS IN THE ABSENCE OF EPINEPHRINE

GEORGE J. WITTENSTEIN, M.D.*

Denver, Colo.

The insulin test as a measure of adrenal cortical function, first described by Fraser and associates[4] in 1941, gained in importance, when Vogt[18] discovered that insulin acted as a stressing agent comparable to epinephrine. Since then it has been used more and more for this purpose in experimental as well as clinical work.[6, 11, 15] It was generally assumed that insulin was a direct stressing agent. Recently the validity of this concept has been challenged by several authors, especially by Gershberg and Long[5] and by Dury,[3] who submitted the theory that neither the insulin nor the hypoglycemia caused by it are the stressing factors, but that in reality the insulin hypoglycemia causes an increased discharge of epinephrine which in turn stimulates the anterior pituitary. This direct action of epinephrine on the anterior hypophysis (via the hypothalamus) to secrete ACTH is a well established fact.[1, 2, 12, 15] The pituitary then in turn stimulates the adrenal cortex. This occurs even if the adrenal is denervated, as Vogt[19, 20] and others [7, 10] have shown. Is epinephrine necessary for the production of the stress reaction to insulin? It seemed worthwhile to attempt to settle this question one way or the other.

MATERIAL AND METHODS

A complete left adrenal medullectomy was done in 3 mongrel dogs, followed approximately three weeks later by a right adrenalectomy, thus leaving the animals without adrenal medullary tissue. After complete recovery they were subjected to intravenous insulin tests, using 0.15 units of regular insulin per Kg. of body weight. A total sympathectomy was then done in 2 of the dogs and the insulin tests were repeated. As a standard measurement of adrenal response to insulin effected stress, the number of circulating eosinophils was determined before and 4 hours after insulin injection, using the Thorn method. Blood sugar values were determined at 0, 15, 30, 45, 60, 90 minutes and 4 hours after injection of insulin.

RESULTS

All three dogs showed a marked and significant eosinopenia 4 hours following insulin injection (table I). The blood sugar curves were characteristic of insulin induced hypoglycemia (chart 1). After total sympathectomy insulin caused eosinopenia of a comparable range (table I), and there was practically no change in blood sugar curves (chart 1).

* From the Department of Surgery and the Halsted Laboratory for Experimental Surgery, University of Colorado School of Medicine, Denver, Colorado.

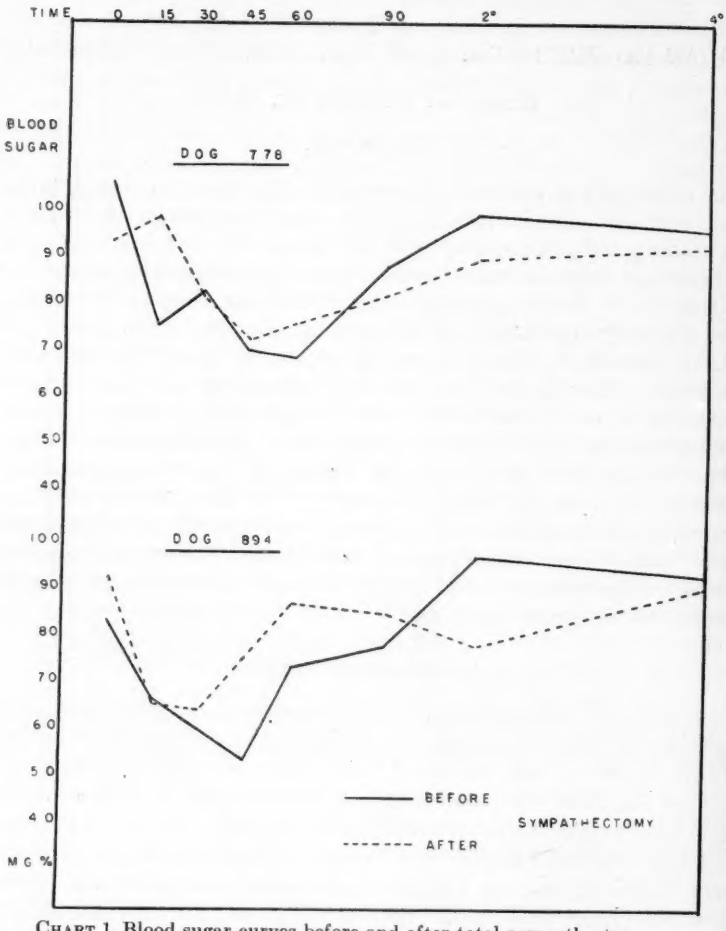


CHART 1. Blood sugar curves before and after total sympathectomy

TABLE I

The per cent decrease in circulating eosinophils 4 hours after administration of 0.15 units of insulin per Kg. is shown. No significant change following medullectomy or later total sympathectomy was observed.

Dog No.	Before Operation	After Adrenal Medullectomy	After Total Sympathectomy
	%	%	%
691	−58	−54	—
778	−64	−58	−56
894	−51	−65	−54

DISCUSSION

If the nonspecific stress following insulin injection were due to an increased discharge of epinephrine, the removal of the adrenal medulla should abolish the adrenal cortical response to insulin as measured by eosinophil counts before and 4 hours after injection. The results of these experiments confirm the fact that adrenal medullectomy in no way interferes with this response, as has been demonstrated by Hume.[9] Vogt[18] found a decrease in adrenal cortical lipids following cold, heat, bleeding and insulin in rats, and this reaction was not prevented by medullectomy. Gordon's later work confirmed these findings.[7] Again in 1951, using the technic of adrenal cortical ascorbic acid determination and measurement of sudanophilic material in the adrenal cortex of the rat, Vogt[19, 20] was able to demonstrate that release of ACTH follows even in the absence of adrenal medullary tissue after insulin administration. If glucose was injected, this response could be greatly reduced but not completely abolished. Thus Vogt concluded that in normal rats the release of ACTH by the pituitary in response to insulin is due to hypoglycemia and epinephrine, while in the medullectomized rat it is a result of the hypoglycemia alone. However, she found that the hypoglycemia itself has no direct effect on the adrenal cortex, since perfusion of the isolated cortex with hypoglycemic blood caused no depletion in ascorbic acid or sudanophilic material. Thus she concluded that the interaction of the hypophysis is required.

That epinephrine is not a necessary factor in eliciting stress has also been shown in an interesting study by Paschkis,[14] in which injection of Dibenamine was followed by a rise in the level of adrenal cortical hormones in the peripheral blood. If insulin was given to dogs previously treated with Dibenamine, the rise in cortical hormone levels was smaller than if only insulin was given. Evidently the epinephrine portion of the stress reaction following insulin injection to normal animals was eliminated by the Dibenamine, although a significant rise in cortical hormone levels still remained.

Our experiments confirm the opinion that the adrenal medulla is not an essential mediator of the stress response to insulin.[16] The possibility remained, however, that enough epinephrine could be discharged from nervous tissue endplates to stimulate the hypothalamo-pituitary system. Therefore, two dogs were completely sympathectomized, eliminating all known sources of epinephrine. In these dogs the same eopenic effect of insulin could clearly be demonstrated.

The fact that Dury came to a different conclusion might be explained by his use of evipal anesthesia in his experiments. It has been shown that many barbiturates suppress the response to stress.[8, 13] Gershberg and Long's experiments were concerned only with the effects of insulin and glucose and did not eliminate the adrenal medulla. Their conclusions, therefore, were not based on actual experimental evidence but were derived solely by deduction.

On the basis of the available experimental data it is apparent that insulin induced stress is augmented, but in no way mediated by the discharge of epinephrine. To what degree adrenal cortical hormones influence the regulation of

blood sugar levels is as yet unknown, but that they play a definite part in it has been shown by Vetter,[17] who was able to demonstrate that desoxycorticosterone acetate has an antidiabetogenic effect in contradistinction to the well known diabetogenic effect of the glucocorticosteroids. As long as we know so little about the exact mechanism controlling blood sugar, we cannot state the site of action of insulin, and we have to assume that the hypoglycemic state *per se* constitutes a systemic, nonspecific stress.

SUMMARY

The insulin test of adrenal cortical function was studied in dogs rendered incapable of elaborating epinephrine by medullectomy and total sympathectomy. The data show that epinephrine is not an indispensable factor in the mechanism of insulin induced stress response.

REFERENCES

1. Dury, A.: Leucocyte picture of rat; relation of adrenal and spleen, Am. J. Physiol. *160:* 75 (Jan.) 1950.
2. Dury, A.: Changes in circulating eosinophiles and adrenal ascorbic acid concentration after agents altering blood sugar levels and other surgical conditions, Am. J. Physiol. *163:* 96 (Oct.) 1950.
3. Dury, A.: Mechanism of insulin-induced eosinopenia in rats, Endocrinology *47:* 387 (Nov.) 1950.
4. Fraser, R. W.; Albright, F., and Smith, P. H.: Value of glucose tolerance test, insulin tolerance test, and glucose-insulin tolerance in diagnosis of glucose metabolism. J. Clin. Endocrinol. *1:* 297 (April) 1941.
5. Gershberg, H., and Long, C. N. H.: Activation of adrenal cortex by insulin hypoglycemia (Abstract) J. Clin. Endocrinol. *8:* 587 (July) 1948.
6. Godlowski, Z. Z.: Eosinopenia caused by adrenaline infusion and by insulin hypoglycemia, Brit. M. J. *1:* 46 (Jan. 10) 1948.
7. Gordon, M. L.: Immediate response of demedullated adrenal gland to stress, Endocrinology *47:* 13 (July) 1950.
8. Hume, D. M., and Wittenstein, G. J.: Relationship of hypothalamus to pituitary-adrenal function, in Proceedings of the First Clinical ACTH Conference 1949. Philadelphia, Blakiston Company, 1950, p. 134.
9. Hume, D. M.: Personal communication to the author.
10. Kahn, R. H., and Münzer, F. T.: Ueber nervös bedingte Veränderungen der Nebennierenrinde während der Insulinvergiftung, Arch. f. d. ges. Physiol. *217:* 521, 1927.
11. Laragh, J. H., and Almy, T. P.: Changes in circulating eosinophils in man following epinephrine, insulin and surgical operations, Proc. Soc. Exper. Biol. & Med. *69:* 499 (Dec.) 1948.
12. Long, C. N. H., and Fry, E. G.: Effect of epinephrine on adrenal cholesterol and ascorbic acid, Proc. Soc. Exper. Biol. & Med. *59:* 67 (May) 1945.
13. Masserman, J. H.: Effects of sodium amytal and other drugs on reactivity of hypothalamus of cat, Arch. Neurol. & Psychiat. *37:* 617 (March) 1937.
14. Paschkis, K. E.; Cantarow, A.; Walkling, A. A., and Boyle, D.: Adrenal cortical hormone levels in adrenal vein and peripheral blood, Endocrinology *47:* 338 (Nov.) 1950.
15. Recant, L.; Forsham, P. H., and Thorn, G. W.: Observations on pituitary-adrenal response following epinephrine infusion in man (abstract) J. Clin. Endocrinol. *8:* 589 (July) 1948.
16. Thorn, G. W.: Diagnosis and Treatment of Adrenal Insufficiency, ed. 2, Springfield, Ill., Charles C. Thomas, 1951, p. 67.
17. Vetter, H.: Über insulin-synergistische Wirkungen des Desoxycorticosteron, Wien. Ztschr. f. Inn. Med. *31:* 361 (Oct.) 1950.
18. Vogt, M.: Cortical lipids of normal and denervated suprarenal gland under conditions of stress. J. Physiol. *106:* 394 (Oct. 15) 1947.
19. Vogt. M.: Hypoglycemia and adreno-cortical secretion, J. Physiol. *113:* 22P, 1951.
20. Vogt, M.: Role of hypoglycemia and of adrenaline in response of adrenal cortex to insulin, J. Physiol. *114:* 222 (June 29) 1951.

ISCHEMIC RENAL EXCRETION IN THE ETIOLOGY OF EXPERIMENTAL RENAL HYPERTENSION*

J. J. LALLY, M.D.

Kansas City, Mo.

The renal origin of hypertension, both in the human subject and in the experimental animal has been a most interesting study since 1934 when Goldblatt produced experimentally renal hypertension by permanently constricting the main renal arteries in dogs.[16] Since then apparently conflicting, but proved, experimental results have given rise to different theories as to the basic etiology of elevated blood pressure.

While it is known that hypertension may develop from different causes in human beings, it is obvious that these causes do not clearly show the etiology of experimental renal hypertension. It is of importance to more clearly define the etiology in the latter, because of the marked similarity between experimental renal hypertension and human essential hypertension,[31, 26, 6, 4, 7, 28] and because the experimental laboratory is the field in which lies our greatest hope of discovering the cause of this widespread disease.

Although numerous theories have arisen regarding the etiology of hypertension, nervous mechanisms as a cause or contributing factor in experimental renal hypertension have been ruled out by the work of several investigators. Page[36] and Collins[9] denervated the kidneys; Goldblatt[17] excised the splanchnic nerves; and complete sympathectomy was done by Alpert, Alving and Grimson.[3] None of these procedures altered or relieved the hypertension created by reducing blood supply to the kidneys.

There are today two main schools of thought on the basic etiology of experimental renal hypertension. The first is that of the renal origin of a substance which initiates the mechanism producing an elevation in blood pressure.[37] This renal substance, named renin by Tigerstedt, and present in press juice of the kidney, is said to enter the circulation via the renal vein and act upon hypertensinogen, a plasma globulin normally in the blood, to form hypertensin, a polypeptide which is the active vasoconstrictor effecting increased resistance of the peripheral vascular bed.[20] The existence of renin is certain,[24] but whether it is the initiator of a high blood pressure mechanism of permanence is in doubt, because it is demonstrable only when blood pressure is rising—as in eclampsia or acute glomerulonephritis—in the human being; it is not demonstrable in benign essential hypertension[12] nor in experimental animals that have had their pressures stabilized at an elevated level for six months or more.

The second is that of Grollman and associates[21] that the kidney is the source of a substance, the absence, destruction or neutralization of which results in hypertension. Grollman has shown that elevated blood pressure is produced in

* Presented as exhibit before Kansas City Southwest Clinical Society Conference September 28, 1953.

dogs subjected to bilateral nephrectomy when they are kept alive by peritoneal lavage. Such reliable investigators as Blalock[7] and Goldblatt[20] have frequently stated, as late as 1947, that *bilateral nephrectomy does not produce any elevation in blood pressure*. However, they did not use Grollman's peritoneal lavage, as a form of artificial kidney.[23] Elevated blood pressure after bilateral nephrectomy has now been produced by several other authors,[30, 34] although each had to use some form of peritoneal lavage or infusion of fluid and electrolyte with the bilateral nephrectomy to induce the higher pressure.

There is difference of opinion at present concerning the mechanism involved in raising the blood pressure in the bilaterally nephrectomized animal. Grollman believes, as previously stated,[21] that *loss of kidney tissue means loss to the body of a substance from the kidney, which keeps pressure normal*, while Orbison and coworkers[34] believe *retention of lavage fluid or injected electrolyte solution is responsible for the elevation of pressure*. On one point, bilateral nephrectomy investigators seem to agree. This form of experimental hypertension cannot be caused by renin in any way, because all kidney tissue is removed from the body. It is well to note at this point, that the histologic alterations in hypertensive animals with bilateral nephrectomy are similar to those described in other reports on malignant hypertension and suggests the possibility of a similar underlying mechanism.[34]

These two ideas admit of no compromise on theoretical grounds, because the first demands the *presence* of a kidney product and the other demands the *absence* of a kidney product, in the development of a higher blood pressure.

RATIONALE OF EXPERIMENTS

In studying the essential work done in this field an attempt has been made to find a common denominator in what appears to be contradictory evidence. One apparent possibility that can apply to the ischemic kidney of Goldblatt, and the bilaterally nephrectomized dog of Grollman, is a disturbance produced by the removal of normal urinary constituents from the organism.

This viewpoint of kidney responsibility for excessive retention or excretion of urine constituents as a factor in the production of elevated blood pressure, brings up two possible considerations:

1. There is too little excretion of some urinary constituent. This would be concluded from the viewpoint that the *ischemic* or *absent*—with lavage—*kidneys* fail to remove from the blood stream a normal quantity of some—as yet unsuspected—substance excreted usually at normal or higher intrarenal pressures. This possibility has already been well studied.[4, 14, 22]
2. There is too much excretion of some urinary constituent relative to others. This conclusion comes from the viewpoint that the *ischemic* or *absent*—with lavage—*kidneys* may selectively remove from the organism too large a quantity of a low threshold substance necessary to the organism to maintain a low or normal blood pressure.

Since Grollman and others have shown that hypertensive animals have disturbed levels of electrolyte in the body, and since the kidney is a logical suspect

in effecting such a disturbance through faulty excretion, we have undertaken experiments to determine exactly what effect urinary excretion has upon hypertension.

The following well known facts were observed preparatory to our experiments: When one kidney is made ischemic by any one of the methods of Goldblatt, Grollman or Page, blood pressure rises usually for a period of four to six weeks and then returns to its former level. The lowering and maintainance of the pressure at the former level, is attributed to the presence of the second normal kidney, because its removal—or *being rendered ischemic*—returns the organism to the hypertensive state.

If urinary excretion has any effect upon blood pressure, the urine from the second kidney in its *normal* or *ischemic* state should—upon reintroduction into the body—show this effect. It was therefore, decided to reintroduce into the organism the urine from the second kidney in both its *normal* state and again in an *ischemic* state, by means of uretero-jejunostomy as shown in figure 1.

Two sets of experiments with controls were necessary: the first one for con-

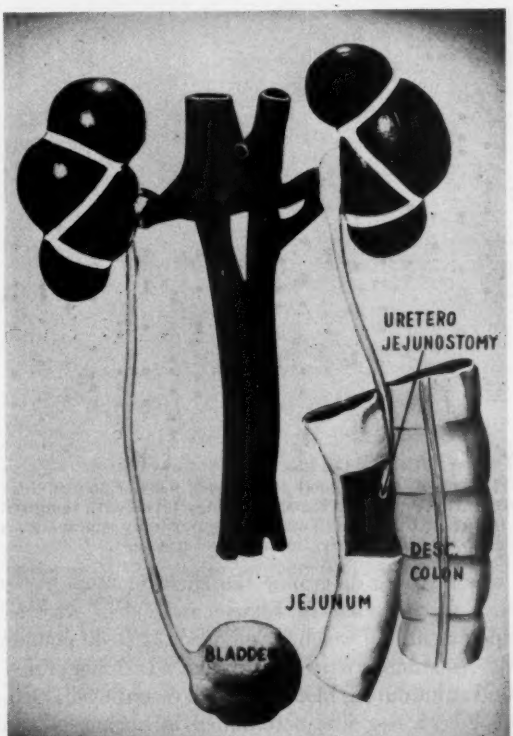
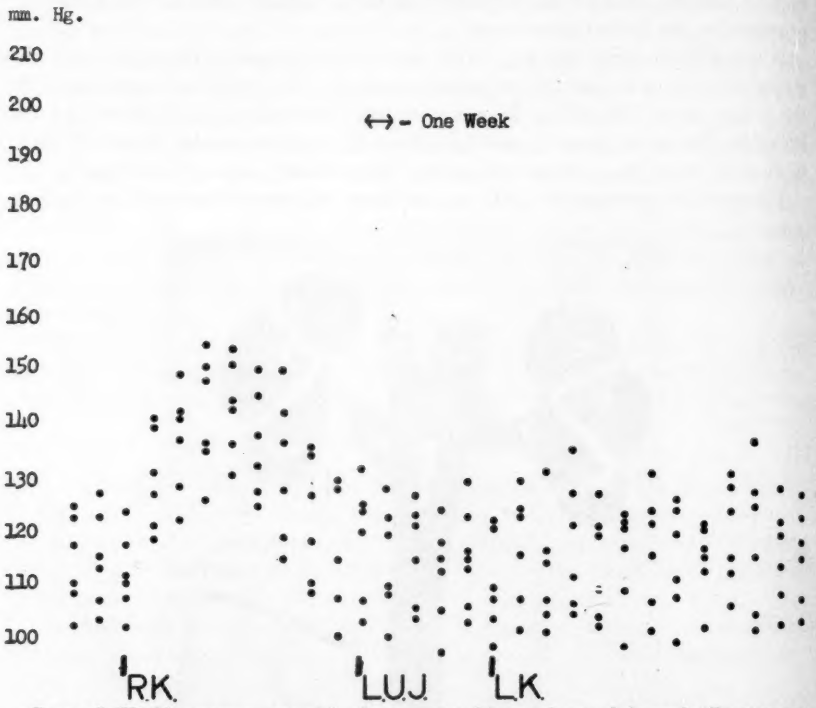


FIG. 1. Ureterojejunostomy for resorption of excretion from one *ischemized* kidney. Suturing to adjacent descending colon reinforces and anchors anastomosis.

tinuous resorption of urine from the second kidney beginning in its *normal* state and continuing as it is put into an *ischemic* state; and, the second, for resorption of urine from the second kidney, after both kidneys have been made *ischemic* and hypertension has already been produced.

MATERIAL AND METHODS

Two series of experiments were planned. Experiment A was made to determine the effect of renal excretion resorption upon the *production of hypertension.*

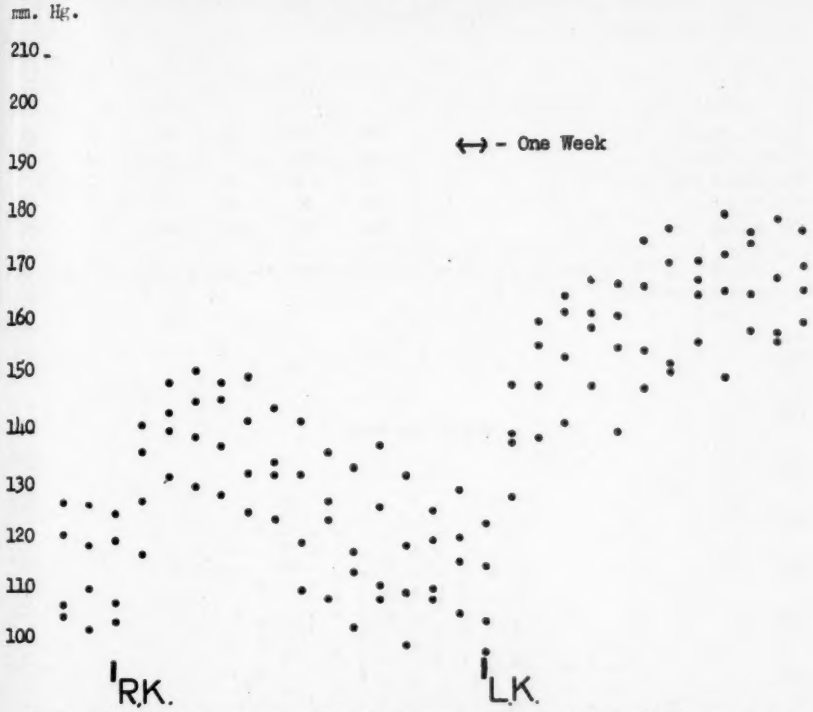


GRAPH I. Weekly average mean blood pressures of 6 experimental dogs via direct puncture method of femoral artery. At R. K., right kidney taped with temporary blood pressure elevation following. At L. U. J., a left uretero-jejunostomy was made. At L. K., the left kidney taped, with no significant elevation of blood pressure.

Experiment B was made to determine the effect of renal excretion resorption upon *hypertension already produced.* Sixteen male dogs were selected for size, weight and temperament. All weights were from 32 to 40 pounds, with an average of 35 pounds. All animals were put through a training period of three weeks to obtain habitual calm during blood pressure recordings. During this time the blood pressure for each dog was determined by means of a direct recording mercury manometer connected with a heparin* solution filled cannula attached to a needle inserted into the femoral artery.

* Heparin used in these experiments was furnished by the Lederle Laboratories.

In Experiment A, 6 experimental dogs and 4 controls were subjected to *figure of eight* ligature of the right kidney. Nine weeks later, when the temporary hypertensive response had subsided, the 6 experimental animals had a left sided uretero-jejunostomy made. Blood pressure recordings were continued daily for five weeks. The 6 experimental and 4 control dogs were then all subjected to *figure of eight* ligature of the right kidneys. Intravenous pyelograms were made



GRAPH II. Weekly average mean blood pressures of 4 control dogs via direct puncture method of femoral artery. At R. K., right kidney taped with temporary elevation of blood pressure following. At L. K., the left kidney taped with subsequent persistent elevation in blood pressure.

to determine patency of the uretero-jejunostomies. Blood pressure recordings were continued for 12 weeks.

In Experiment B, the experimental dogs were subjected to a *figure of eight* ligature of both kidneys, six weeks apart. Controls were the same 4 animals used as controls in Experiment A, except that they were now *hypertensive*. When the blood pressure became stabilized—12 weeks—the 6 experimental animals were subjected to a left sided uretero-jejunostomy while the 4 control animals had left nephrectomies. Blood pressure recordings were continued for 10 weeks. At the end of each experiment the experimental animals were killed for micro-

TABLE 1

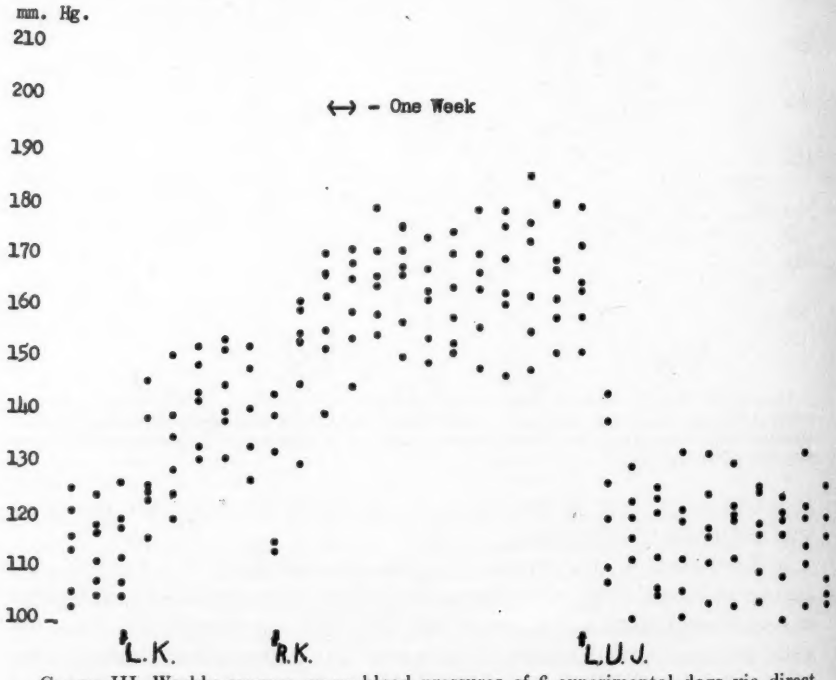
Experimental Group A

	Dog					
	1	2	3	4	5	6
N.P.N. (mg.%)	44	53	34	39	33	41
Urea N. (mg.%)	12	18	14	15	16	21
Creat. (mg.%)	.9	.1	1.3	1.1	1.4	1.1
CO_2 (vol.%)	46	55	51	57	50	58
Cl (mg.%)	458	508	517	510	580	464

Experimental Group B

	Dog					
	11	12	13	14	15	16
N.P.N. (mg.%)	30	44	40	36	28	32
Urea N. (mg.%)	12	14	17	15	16	13
Creatinine (mg.%)	.8	1.2	.9	1.7	.7	1.
CO_2 (vol.%)	55	64	46	52	49	54
Cl (mg.%)	554	494	560	525	612	550

Composite of blood chemistry findings in Experimental Groups A and B. All have had uretero-jejunostomies.

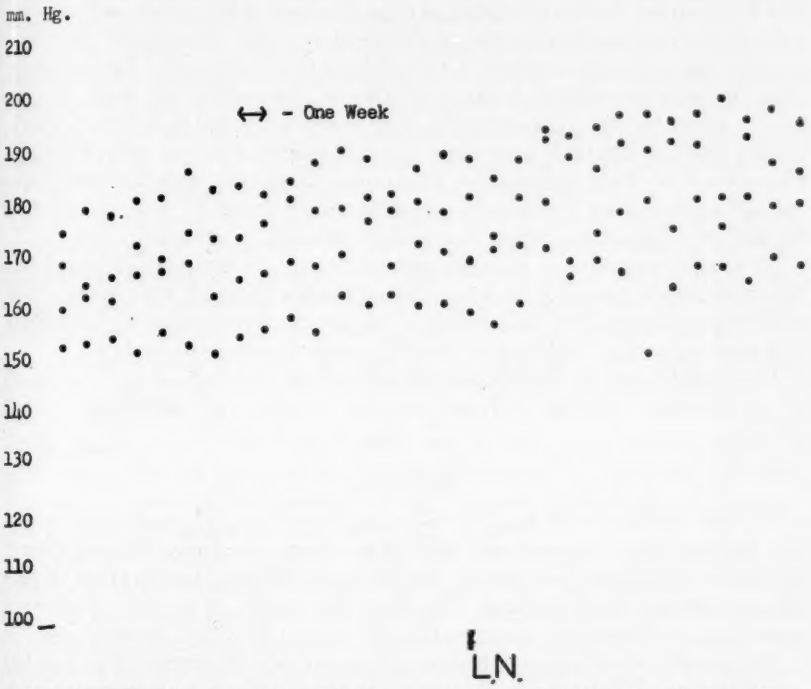


GRAPH III. Weekly average mean blood pressures of 6 experimental dogs via direct puncture method of femoral artery. At L. K., left kidney taped with temporary blood pressure elevation following. At R. K., right kidney taped with permanent type elevation of blood pressure following. At L. U. J., left uretero jejunostomy was made with following reduction of blood pressure to preoperative levels.

scopic study of the liver and adrenal glands. Blood studies made at the end of each experiment included non-protein nitrogen, urea, CO_2, chlorides and creatinine.

RESULTS

In Experiment A, in which one kidney was made ischemic by the Grollman method, we found that rendering the second kidney ischemic did not produce hypertension if a uretero-jejunostomy had been done beforehand.



GRAPH IV. Weekly average mean blood pressures of 4 control dogs via direct puncture method of femoral artery. At L. N., a left nephrectomy was done with no significant effect upon blood pressure.

Six animals subjected to a *figure of eight* ligature of the right kidney showed the expected temporary hypertension response for about six weeks. At nine weeks each had a left uretero-jejunostomy made, and as noted, all pressures continued at nearly the same as their original values for five weeks. Finally the 6 animals were subjected to *figure of eight* ligature of the left kidneys, the ureters of which entered the jejunum. Graph I shows no appreciable change in blood pressure over a 12 week period.

While our control animals all developed the expected rise in blood pressure with bilateral kidney ligation, as seen in graph II, the experimental animals

having uretero-jejunostomies plus bilateral kidney ligation did not develop rises in blood pressure.

Our 6 experimental animals were all in good general condition, ate well and evidenced no outward sign of disease. The blood findings on these animals, as seen in table I, were within normal limits, including the blood urea. Microscopic study of the livers and adrenal glands revealed no pathologic findings of any kind in these 6 animals.

In Experiment B, in which both kidneys were made ischemic by the Grollman method and an expected resultant hypertension produced, we found that uretero-jejunostomy, for the resorption of urine from one of the ischemized kidneys, reduced the hypertension to original preoperative levels. Six animals were subjected to *figure of eight* ligatures of both kidneys six weeks apart. Twelve weeks after the second operation, a left sided uretero-jejunostomy was made and, as seen in graph III, the mean pressures of all animals dropped to near pre-experimental levels in less than three days. Control animals were the same 4 used in Experiment A. They entered the Experiment B period, with previously developed hypertension. The control pressures seen in graph IV were not affected by the left nephrectomy other than a slight increase in pressure.

All animals appeared in good general condition, ate well and all completed the experimental period in 31 weeks. Blood studies on the 6 experimental animals of Experiment B, including blood urea, non-protein nitrogen, CO_2, chloride and creatinine were within normal limits as seen on composite table I.

Microscopic study of the liver and adrenal glands revealed—as in Experiment A—no pathologic findings in these 6 animals, except a very mild hepatitis in 2 of them.

DISCUSSION

The full significance of renal excretion upon experimental renal hypertension has not been fully demonstrated until this experiment. Dragstedt and Geer,[14] Grollman[22] and others have shown that resorption of urine has no effect in producing elevated blood pressure. This they have shown in a most satisfactory manner by ureteroenteric anastomosis and ureterovena caval anastomosis.[25]

The vasodepressor action of resorbed urine from the hypertensive animal has not been studied. Existence in the urine of both pressor and depressor substances has been known for some time[1, 2] and Page[35] has demonstrated these effects in cats, but the idea of the hypertensive organism, being unable to retain a normal vasodepressor because of faulty renal excretion, is not to be found in experimental work in this field.

For purposes of comparison and elucidation this paper demonstrates the *effect of renal excretion resorption both on the production of experimental renal hypertension and upon such hypertension already produced.*

As seen from graphs I and II, permanent experimental renal hypertension cannot be produced in the dog if a functioning uretero-jejunostomy has already been made. Control animals, similarly treated with bilateral *figure of eight* ligatures of the kidneys, but without uretero-jejunostomy, developed the expected hypertension.

Graphs III and IV in Experiment B, demonstrate that existent experimental renal hypertension, is alleviated by uretero-jejunostomy. That this effect is brought about by resorption of urine is further confirmed by negative results in the control animals subjected to nephrectomy rather than uretero-jejunostomy.

The lowering and prevention of hypertension by resorption of ischemic renal excretion leads to a conclusion which is obvious. The conclusion is that, at least in experimental renal hypertension, the *ischemic kidneys are excreting a substance or substances hereinafter referred to as U.V.D.—urinary vaso depressor—necessary to the body to maintain normal blood pressure.*

A logical question would be, *why does removing the kidney fail to produce the same lowering of pressure as resorbing its total excretion by uretero-jejunostomy?* The answer is seen in the conclusion that *the kidney in both the normal and ischemic state is the seat of origin of a vasodepressor substance or initiator which is necessary to the body to maintain normotensive pressure.* The ischemic kidney excretes this substance as shown by the above experiments.

Therefore, removal of one of two ischemic kidneys should cause no lowering of pressure, as the remaining ischemic kidney continues to excrete. However, removal of one ischemic kidney, when the other is normal should reduce the blood pressure to normal or near normal. In support of this idea is Goldblatt's[18] work in which removal of one ischemic kidney, quickly reduced even the temporary hypertension it produced when intact. Also there are many clinically reported cases in which unilateral nephrectomy has abolished hypertension in human beings.[5, 33, 32, 29, 15, 39, 11]

The absorbed urine does not, upon entering the portal system, create, a hepatitis to lower the pressure, as was claimed possible by Davis and Tanturi.[10] Microscopic study of the livers of our experimental animals revealed a very mild degree of inflammatory reaction in only 2 cases.

The only reasonable conclusion drawn from these 2 experiments is that *the ischemic kidneys, in producing experimental renal hypertension, excrete from the organism a U.V.D., formed in the renal tissue itself, which, if absorbed via the intestinal tract by means of a uretero-jejunostomy, will make the production or maintainance of this type of hypertension as difficult to achieve as if one kidney were still normal.*

These experiments would seem to support our idea that a disturbance in renal excretion is the primary factor in experimental renal hypertension. Although renin must certainly be recognized as a substance of vast physiologic significance in the field of hypertension, especially after the work of Houssay,[27] Braun-Menendez,[8] Fasciolo,[13] Taquini,[40] Page,[38] Goldblatt and others,[19] our evaluation of its specific importance in causing hypertension is low because of the following elementary rationale.

In raising the blood pressure in experimental renal hypertension, the kidney has only three possible roles.

1. Give to the body a new substance, a combination of substances, or more of a substance normally given to the body. (Renin Theory)
2. Stop giving to the body a substance normally given to it, or at least give

this substance in less than normal quantities (hypertension with bilateral nephrectomy).

3. Remove from the body a substance or group of substances, without which, the body develops hypertension. (Our urinary vasodepressor excretion idea.)

Examining these three possibilities:

1. The renin theory cannot explain experimental hypertension in the absence of both kidneys as produced by Grollman, Orbison and others. Hence we conclude that renin is not necessary as the primary factor of initiating hypertension, although it no doubt is of significant secondary importance.
2. Bilateral nephrectomy alone does not cause a rise in blood pressure according to most investigators. It is only after peritoneal lavage or infusion of water or electrolyte solutions that hypertension develops in the bilaterally nephrectomized animal. Hence the mere removal of the kidneys alone is not enough to cause hypertension.
3. Only after low pressure removal from the organism of supposed urinary waste products, does this form of hypertension develop, (or dilution of such substances within the body).

The ischemic kidney with a Goldblatt clamp is admittedly a low pressure kidney and external compression in any form must be regarded as effecting a lower pressure gradient in the internal hemodynamics of the renal tissue. Peritoneal lavage is a form of low pressure artificial kidney; and infusion of fluids, while not removing anything from the organism, certainly causes a dilution of all freely circulating substances in the body.

Support of such conclusions is seen in the vasodepressor action of resorption of ischemic renal excretion.

It seems apparent that the vasodepressor substance excreted by the ischemic kidney, comes from the renal tissue itself, because in an animal with both kidneys ischemized a uretero-jejunostomy, in effecting total absorption of excretion from one kidney, returns blood pressure to normal, while removal of the same kidney, instead of uretero-jejunostomy does not lower the blood pressure at all.

SUMMARY

The vasodepressor action of resorption of excretion from the so called ischemic kidney, is demonstrated by continuous absorption of urinary excretion from one of two kidneys made ischemic by the Grollman method.

Explanation of such blood pressure reducing results after uretero-jejunostomy cannot be explained readily on the rationale of the renin theory, or completely explained by the present day rationale of hypertension following bilateral nephrectomy with peritoneal lavage or infusion of fluids and electrolytes.

It seems most probable that vasodepression through resorption of ischemic renal excretion via uretero-jejunostomy in the hypertensive animal is accomplished by the reabsorbing of a urinary vasodepressor (U.V.D.) manufactured at least partially within the kidney itself and which is excreted by the ischemic, but not the normal kidney.

The surgical construction of a patent, functioning uretero-jejunostomy was possible only after a well worked out technic, including intravenous pyelograms for postoperative evaluation of patency of the ureteral orifice in the jejunum. Obstruction, total or partial of the involved ureter prevents the vasodepressor results of such a procedure and in some cases will tend to raise the blood pressure.

CONCLUSIONS

Resorption of ischemic renal excretion has a vasodepressor action in experimental renal hypertension in dogs. Excessive renal excretion of a vasodepressor, formed at least partially by the kidney itself, is concluded to be a primary factor in the etiology of experimental renal hypertension. Uretero-jejunostomy has been found to be a most effective means of producing resorption of renal excretion.

REFERENCES

1. Abelous, J. E., and Bardier, E.: Action hypertensive de l'urine de l'homme normal; premières recherches sur l'urohypertensine, J. de physiol. et de path. gén., Par., *10:* 627, 1908.
2. Abelous, J. E., and Bardier, E.: L'urohypertensine, J. de physiol. et de path. gén., Par., *11:* 34, 1909.
3. Alpert, L.; Alving, A. S., and Grimson, K. S.: Effect of total sympathectomy on experimental renal hypertension in dogs, Proc. Soc. Exper. Biol. & Med. *37:* 1 (Oct.) 1937.
4. Baird, J. S.; Scott, R. L., and Spencer, R. D.: Studies on transplantation of ureters into intestines, Surg., Gynec. & Obst. *24:* 482, 1917.
5. Barker, N. W., and Walters, W.: Hypertension and chronic atrophic pyelonephritis, J.A.M.A. *115:* 912 (Sept. 14) 1940.
6. Beckwith, J. R., and Chanutin, A.: Blood volumes in hypertensive partially nephrectomized rats, Proc. Soc. Exper. Biol. & Med. *46:* 66 (Jan.) 1941.
7. Blalock, A., and Levy, S. E.: Studies on etiology of renal hypertension, Ann. Surg. *106:* 826 (Nov.) 1937.
8. Braun-Menendez, E.; Fasciolo, J. C.; Leloir, L. F., and Munoz, J. M.: Substance causing renal hypertension, J. Physiol. *98:* 283 (July 24) 1940.
9. Collins, D. A.: Hypertension from constriction of arteries of denervated kidneys, Am. J. Physiol. *116:* 616 (Aug.) 1936.
10. Davis, L., and Tanturi, C. A.: Liver as factor in experimental renal hypertension, A.M.A. Arch. Surg. *62:* 325 (March) 1951.
11. Dean, A. L., and Abels, J. C.: Study by newer renal function tests of unusual case of hypertension following irradiation of one kidney and relief of patient by nephrectomy, J. Urol. *52:* 497 (Dec.) 1944.
12. Dexter, L., and Haynes, F. W.: Relation of renin to human hypertension with particular reference to eclampsia, preeclampsia and acute glomerulonephritis, Proc. Soc. Exper. Biol. & Med. *55:* 288 (April) 1944.
13. Fasciolo, J. C.; Houssay, B. A., and Taquini, A. C.: Blood-pressure raising secretion of ischemic kidney, J. Physiol. *94:* 281 (Dec. 14) 1938.
14. Geer, W. A., and Dragstedt, L. R.: Studies on renal hypertension; effect of deviating urine into blood stream and intestines of dogs, Ann. Surg. *108:* 263 (Aug.) 1938.
15. Gibson, T. E.: Hypertension and surgical kidney, California & West. Med. *56:* 66 (Feb.) 1942.
16. Goldblatt, H.; Lynch, J.; Hanzal, R. F., and Summerville, W. W.: Studies on experimental hypertension: production of persistent elevation of systolic blood pressure by means of renal ischemia, J. Exper. Med. *59:* 347 (March) 1934.
17. Goldblatt, H., in Proc. Assn. Path. and Bact., Boston April 9–10, 1936.
18. Goldblatt, H.: Studies on experimental hypertension; pathogenesis of experimental hypertension due to renal ischemia, Ann. Int. Med. *11:* 69 (July) 1937.
19. Goldblatt, H.; Katz, Y. J.; Lewis, H. A., and Richardson, E.: Studies on experimental hypertension: bioassay of renin, J. Exper. Med. *77:* 309 (April) 1943.
20. Goldblatt, H.: Renal origin of hypertension, Physiol. Rev. *27:* 120 (Jan.) 1947.
21. Grollman, A.; Harrison, T. R., and Williams, J. R., in Proc. Am. A. Adv. Sci. *13:* 274, 1940.
22. Grollman, A.; Muirhead, E. E., and Vanatta, J.: Role of kidney in pathogenesis of hypertension as determined by study of effects of bilateral nephrectomy and other experimental procedures on blood pressure of dog, Am. J. Physiol. *157:* 21 (April) 1949.

23. Grollman, A.: Personal communication to the author, 1952.
24. Grossman, E. B.: Preparation of extracts of renal pressor substance, Proc. Soc. Exper. Biol. & Med. *39:* 40 (Oct.) 1938.
25. Hinman, F., and Belt, A. E.: Experimental study of ureteroduodenostomy, J.A.M.A. *79:* 1917 (Dec. 2) 1922.
26. Holman, D. V., and Page, I. H.: Cardiac output in arterial hypertension, Am. Heart J. *16:* 321 (Sept.) 1938.
27. Houssay, B. A.; Braun-Menendez, E., and Dexter, L.: Destruction and elimination of renin in dog, Ann. Int. Med. *17:* 461 (Sept.) 1942.
28. Kapp, F.; Friedland, C. K., and Landis, E. M.: Skin temperature of hypertensive rabbits and pressor effects of heated kidney extracts, Am. J. Physiol. *131:* 710 (Jan.) 1941.
29. Koons, K. M., and Ruch, M. K.: Hypertension in seven year old girl with Wilms' tumor relieved by nephrectomy, J.A.M.A. *115:* 1097 (Sept. 28) 1940.
30. Leonards, J. R., and Heisler, C. R.: Blood pressure of bilaterally nephrectomized dogs, Federation Proc. *11:* 247 (March) 1952.
31. Lorber, V., and Visscher, M. B.: Action of angiotonin on completely isolated mammalian heart, Am. J. Physiol. *133:* 365 (June) 1941.
32. O'Conor, V. J.: Indications and prognosis in unilateral nephrectomy, J.A.M.A. *120:* 579 (Oct. 24) 1942.
33. Oppenheimer, B. S.; Klemperer, P., and Moschkowitz, L.: Evidence for Goldblatt mechanism of hypertension in human pathology, Tr. A. Am. Physicians *54:* 69, 1939.
34. Orbison, J. L.; Christian, C. L., and Peters, E.: Studies on experimental hypertension and cardiovascular disease. 1. Method for rapid production of malignant hypertension in bilaterally nephrectomized dogs, A.M.A. Arch. Path. *54:* 185 (Aug.) 1952.
35. Page, I. H.: Vascular action of fresh urine and extracts thereof, Proc. Soc. Exper. Biol. & Med. *32:* 302 (Nov.) 1934.
36. Page, I. H.: Relationship of extrinsic renal nerves to origin of experimental hypertension, Am. J. Physiol. *112:* 166 (May) 1935.
37. Page, I. H., in Proc. Am. A. Adv. Sc. *13:* 239, 1940.
38. Page, I. H.: Pressor response of normal and hypertensive dogs to renin and angiotonin, Am. J. Physiol. *134:* 789 (Nov.) 1941.
39. Ratliff, R. K., and Conger, K. B.: Incidence of renal hypertension and of cure by nephrectomy, J. Urol. *48:* 136 (Aug.) 1942.
40. Taquini, A. C.: Production of pressor substance by totally ischemic kidney, Am. Heart J. *19:* 513 (May) 1940.

RELIEF OF POSTOPERATIVE PAIN

HARRELL C. DODSON, JR., M.D.
HOWARD A. BENNETT, M.D.

Oklahoma City, Okla.

Some of the complications that occur following operations may be caused, precipitated or aggravated by drugs used to combat postoperative pain. While such undesirable effects of analgesics are usually the result of excessive dosage, minor degrees of morbidity due to such drugs are so common that they are customarily accepted as a matter of course.

Recognizing the role of psychosomatic factors in human illness and the placebo action of therapeutic measures, a clinical study was instituted in an effort to determine the incidence of pain following various types of major surgery, the amount of analgesic drug necessary to allay postoperative pain and the influence of certain factors on the frequency and severity of postoperative pain.

METHOD OF STUDY

In a series of 335 consecutive major operations done on adult patients at The University of Oklahoma Hospital, postoperative pain was treated by injection of placebos. The nurses on the surgical wards were instructed to ascertain the effect of each placebo 10 to 15 minutes after injection and to administer an appropriate analgesic if the placebo was not effective. Meperidine in doses of 25 to 100 milligrams was, with few exceptions, the analgesic agent used. When other drugs were used, they were recorded, for the purpose of the study, as meperidine in equivalent dosage. In each case, the total quantity of meperidine given during the seven days following operation was considered the postoperative analgesic requirement. Hypnotics were not used.

For control, the postoperative analgesic requirements of 270 patients who had abdominal or thoracic operations during a period immediately prior to the study were determined.

RESULTS OF STUDY

The total analgesic requirements are presented in table I. Thirty per cent of the patients received nothing for postoperative pain. An additional 15 per cent received nothing except placebos. Only 55 per cent required one or more injections of a pharmacologically active agent for relief of postoperative pain. More than half of these patients received a total dose of meperidine of 100 milligrams or less. Only 6 per cent of the patients required a quantity of meperidine exceeding 300 milligrams.

For more detailed study, the patients were divided into two categories, namely,

From the Department of Surgery and the Department of Anesthesiology, University of Oklahoma School of Medicine, Oklahoma City, Oklahoma.

Presented during the annual assembly of The Southwestern Surgical Congress, Salt Lake City, Utah, Sept. 21–23, 1953.

those having abdominal and thoracic operations, and those having operations on other anatomic sites. The types of operations included in each category are listed in table IIA and IIB. In table III the analgesic requirements for the two categories are compared. Thirty-two per cent of those who had abdominal or thoracic operations and 62 per cent of those who had other types of surgery required no meperidine during the postoperative period. Only 9 per cent of those

TABLE I

Placebo study: postoperative analgesic requirements

	Total No. Cases	Total Quantity of Meperidine Required				
		None	Placebo only	25–100 Mg.	100–300 Mg.	Over 300 Mg.
No. of cases	335	101	49	101	101	20
Per cent	100	30	15	30	19	6

TABLE II

Type of Operation	No. of Cases
A. Types of operations: abdominal and thoracic	
Biliary tract and pancreas	40
Gastric resection	38
Appendectomy	19
Thoracic and thoraco-abdominal	15
Colon resection	13
Inguinal hernioplasty	13
Ventral hernioplasty	12
Small intestinal resection	10
Lumbar sympathectomy	8
Closure of perforated viscus	6
Splenectomy	4
Miscellaneous	16
Total	194
B. Types of operations: other sites	
Anorectal operations	27
Thyroidectomy	15
Radical neck dissection	9
Radical neck dissection combined with resection of jaw, etc.	8
Other radical operations for cancer of face and mouth	11
Other neck operations	8
Radical mastectomy	14
Other operations on breast	15
Major amputations	9
Other operations on extremities	13
Plastic operations	12
Total	141

in the former group and 1.4 per cent of those in the latter group required a total dose of meperidine of over 300 milligrams.

In table IV, the postoperative analgesic requirements in four groups of patients who had abdominal or thoracic operations are listed. Patients in the first and second groups received placebos for postoperative pain; those in the third and fourth groups did not. Patients in the second and third groups had unilateral or bilateral intercostal blocks with nupercaine in oil at the time of operation. In the placebo groups, 64 per cent and 77 per cent, respectively, required meperidine; in the two groups that did not receive placebos, 95 per cent and 98 per cent, respectively, required meperidine. In the placebo groups, only 7 per cent and 15 per cent, respectively, needed over 300 milligrams of meperidine, while in the two groups that did not receive placebos, 52 per cent and 59 per cent, respectively, needed over 300 milligrams of the drug.

The observations presented in table IV do not represent a critical appraisal of the effectiveness of intercostal nerve block, since, in this study, blocks were done only in selected cases. We are, however, conducting a study of intercostal block. A preliminary survey of the results of that study supports the reports of others[2] regarding the effectiveness of the procedure in reducing pain after abdominal and thoracic operations.

In this group of patients, the influence of such factors as age, sex and body

TABLE III

Analgesic requirements according to type of operation

Total Quantity Meperidine Required	Abdominal & Thoracic		Other Sites	
	No. of Cases	Per cent	No. of Cases	Per cent
None	37	19	64	45
Placebo *only*	25	13	24	17
25–100 mg.	67	34	34	24
100–300 mg.	47	24	17	12
Over 300 mg.	18	9	2	1.4
Total	194		141	

TABLE IV

Analgesic requirements: abdominal and thoracic operations

Meperidine, Total Quantity Required	Placebo without Intercostal Block		Placebo with Intercostal Block		Intercostal Block without Placebo		Neither Block nor Placebo	
	No. Cases	Per cent	No. Cases	Per cent	No. Cases	Per cent	No. Cases	Per cent
None	29	22	8	13	8	5	2	2
Placebo *only*	19	14	6	10	—	—	—	—
25–100 mg.	47	35	20	33	19	12	8	8
100–300 mg.	29	22	18	30	52	31	33	31
Over 300 mg.	9	7	9	15	86	52	62	59
Total	133	100	61	100	165	100	105	100

build on postoperative pain and analgesic requirements was not significant. There was no apparent difference between the analgesic requirements of charity patients and those of private patients. The variations in the anesthetic and operative technics used in each type of operation were too minimal to permit an evaluation of the influence of those factors on postoperative pain.

Throughout the period of study, it was evident that the quality of nursing care exerted a definite influence on postoperative pain. On the wards that were staffed by an adequate complement of efficient and sympathetic nurses, both the frequency and severity of postoperative pain were noticeably lower than those on the wards that were understaffed or poorly staffed. The reciprocal effect of the study program on the quality of nursing care was also apparent. When the nurses learned, from their own observations, that postoperative pain was not inevitable and that it often could be relieved by placebos, they became more discriminate in their use of narcotics and exhibited more interest in the application of nursing technics to allay apprehension and discomfort.

DISCUSSION

Our observations regarding the frequency of postoperative pain are similar to those reported by Papper, Brodie and Rovenstine[3] who, while investigating the analgesic activity of a new compound, found that about one-third of the patients did not have postoperative pain sufficiently severe to elicit a complaint and that many of those who did complain of pain obtained relief with administration of placebos.

It is interesting to compare our findings with those of Beecher[1] in his study of pain in freshly wounded soldiers. Although they had received no morphine for a matter of hours, three-fourths of those severely wounded men had so little pain that they did not want analgesic medication. When questioned as to the severity of pain, 32 per cent stated that they had no pain, 25 per cent had slight pain, 18 per cent had moderate pain and 24 per cent had severe pain. Certainly, the pain resulting from battle wounds is often diminished or blocked entirely by the strong emotional factors incident to such wounds. Apparently the pain resulting from surgical wounds can be modified in the same direction, although not in the same magnitude, by a simple psychotherapeutic measure such as the administration of placebos.

SUMMARY

In a series of 335 major operations, postoperative pain was treated by placebos. When placebos were not effective, meperidine was given in quantities sufficient to provide relief.

Thirty per cent of the patients received no therapy for postoperative pain. An additional 15 per cent obtained relief with placebos. Fifty-five per cent required one or more injections of meperidine. Only 6 per cent required a total dosage of this drug of over 300 milligrams.

Sixty-eight per cent of patients who had abdominal or thoracic operations required meperidine; 9 per cent received a total amount of over 300 milligrams.

Only 38 per cent of patients who had operations on other sites needed meperidine; the total dose exceeded 300 milligrams in only 1.4 per cent.

In a group of patients who had abdominal or thoracic operations prior to the placebo study program, over 95 per cent required meperidine. More than half of these patients received over 300 milligrams of the drug.

CONCLUSIONS

Abdominal and thoracic operations generally cause more postoperative pain than operations on other regions of the body. Other somatic factors such as magnitude of operation, sex and body type of the patient do not influence the severity of postoperative pain to a significant degree.

Postoperative pain rarely is severe enough to justify administration of analgesics in quantities sufficient to produce undesirable side effects.

Because of the profound influence of emotional factors on postoperative pain, the placebo action of medication given for relief of pain may be more important than the pharmacologic action of the drug. An understanding of that fact by those caring for postoperative patients will eliminate injudicious use of narcotics and will tend to improve the quality of postoperative care.

REFERENCES

1. Beecher, H. K.: Pain in men wounded in battle, Ann. Surg. *123:* 96 (Jan.) 1946.
2. Deaton, W. R., Jr., and Bradshaw, H. H.: Relief of postthoracotomy pain, Surg., Gynec. & Obst. *97:* 140 (Aug.) 1953.
3. Papper, E. M.; Brodie, B. B., and Rovenstine, E. A.: Postoperative pain; its use in comparative evaluation of analgesics, Surgery *32:* 107 (July) 1952.

CEREBELLAR HEMANGIOMAS; A CLINICO-PATHOLOGIC STUDY OF FOURTEEN CASES*

J. M. MEREDITH, M.D.
G. R. HENNIGAR, M.D.

Richmond, Va.

INTRODUCTION

This is a report of 14 cases of verified cystic or solid cerebellar hemangiomas seen in our clinic over a consecutive 22 year period (1930 to 1952). Cerebellar hemangioma, also known in the literature as hemangioblastoma (which latter term is not preferred by the present writers for reasons given below), occur in the frequency of 1.25 per cent to 2.0 per cent of any consecutive, unselected large series of verified brain tumors and therefore are to be considered as rather rare intracranial neoplasms. Hicks and Warren[14] utilize the term hemangioma although practically all other writers—past and present—prefer the term hemangioblastoma. Cushing,[7] in his monograph on over 2,000 verified intracranial tumors, reported 25 cerebellar hemangioblastomas of which one was proved at autopsy without preceding operation. They constituted 1.25 per cent of his entire series of verified brain tumors.

In one of the largest series on record, that of Silver and Hennigar,[23] (1952) (40 cases) there was found no predilection for either sex. The highest incidence falls into two age periods, namely, the third and sixth decades. Three of our 14 cases (table I) were in patients aged 14, 19 and 20 while 2 were aged 60 and 61 years. Ford[13] describes a case in some detail of a 15 year old boy with a fatal postoperative lesion—cavernous hemangioma of the cerebellar vermis. Bailey, Buchanan and Bucy[2] (1939) in describing 100 consecutively verified unselected intracranial tumors of infancy and childhood, recorded no instance of hemangioma of the cerebellum in the age group up to the sixteenth birthday included in their book. The average age of our 14 patients was 39.0 years at the time of the first operation or verification at necropsy. Two of the patients were Negroes —both males. The cases were equally distributed as to sex. Erythrocytosis was present in 42.9 per cent of the cases, the highest incidence in the literature to date. This figure is not too reliable, however, as no hematocrit studies, plasma or blood volume determinations, or bone marrow studies were made, hence simple hemoconcentration was not entirely eliminated in any of them. In the study of this series, an arbitrary rule was adopted that any female patient who did not have an erythrocyte count above 5 million per cubic millimeter and any male patient who did not have an erythrocyte count above 6 million per cubic millimeter did not have erythrocytosis. Angiomatosis retinae was found in 2 cases (14.3 per cent)—both Negro males—although it was not specifically

* From the Departments of Neurological Surgery and Pathology, Medical College of Virginia, Richmond, Virginia.
Read at a regular meeting of the Richmond Academy of Medicine, February 26, 1952.

looked for through dilated pupils by expert ophthalmologists, particularly in the earlier cases, and the occurrence of von Hippel's disease could well be considerably higher in our series than the actual percentage here recorded. Furthermore, Danis[10] (1950) stressed that in von Hippel's disease there may be exudates and hemorrhages, massive exudation, retinal detachment and even glaucoma, any of which complications could mask a retinal angioma. Silver and Hennigar[23] noted Lindau's syndrome in 9 of their 40 verified cases (22.5 per cent) but they stressed that possibly many more of their patients had retinal lesions and they were not clinically recognized.

In only 1 of our 14 cases (7.14 per cent) was Lindau's syndrome present in more than one member of a family (case no. 8) and this finding was presumptive and inferential only. Craig and Horrax[5] (1949) and Tonning, Warren and Barrie[24] (1952) report interesting familial instances of the disease.

Six of our 12 surgically verified cases (50 per cent) had more than one surgical attack on their cerebellar lesion. Twelve of the lesions were grossly unilocular cerebellar cysts with a mural nodule; two were solid growths. Twelve of the tumors in our series were surgically verified; two were first demonstrated at postmortem examination and 1 of these last 2 cases was not seen by the neurosurgical department during life (case no. 9—table I). The other had had a negative exploration of the sella (case no. 10—table I) 11 years before death because of a greatly enlarged sella and visual field changes due, very likely, to an internal hydrocephalus incident to the slowly developing cerebellar lesion. This patient died, not of her cerebellar lesion, but primarily due to a severe acute head injury. The cystic cerebellar lesion was a chance finding at necropsy as was a pheochromocytoma. She also had von Recklinghausen's disease of the skin and subcutaneous tissues. In the series reported here there were 2 postoperative deaths in 12 surgically treated patients, or a case mortality rate of 16.7 per cent. However, because of multiple operations in some cases, a total of 19 surgical procedures were carried out, thus the operative mortality was 10.5 per cent.

Another large surgical series of these cases was that of Loyal Davis,[11] who reported his experiences in 1946 with 22 patients. His operative mortality was 22.7 per cent. Dandy[9] in 1928 reported 7 cases of angiomatous cysts of the cerebellum. A report on these lesions by Perlmutter, Horrax and Poppen[22] appeared in 1950 from the Lahey Clinic. They reviewed 25 cases of cystic hemangioma of the cerebellum seen in a 15 year period (1933 to 1948), during which time 1300 brain tumors were also verified (2 per cent). They elected to exclude their cases of solid cerebellar hemangioblastomas in their report. Their operative mortality was 8 per cent (two surgical deaths in 25 cases). In 1952 Olivecrona[21] reported the largest series of this disease on record from a single clinic—70 cases. He designates the lesion as *angioreticuloma*. Cramer and Kimsey[6] reported 53 cases in 1952.

Four of the 25 patients with cystic hemangioblastoma cerebelli of Perlmutter, Horrax and Poppen had angiomas of the retina (16 per cent). Lindau[19] stated that 20 per cent of patients with angiomatosis retinae had central nervous system angiomas. Fourteen of the 25 cases of the Boston group[22] had choked

TABLE I

14 cases of cerebellar hemangioma from the Medical College of Virginia

Case	Sex	Age	Race	Erythrocytosis	Angiomatosis Retinae	Familial History	Number of Operations	Type of Growth	How Verified	Postoperative Deaths	Remarks
1. V. W.	M	14	W	Yes 7,200,000 RBC 130% HB	No	No	2	Cystic	Oper.	0	
2. M. E.	F	51	W	Yes 5,520,000 RBC 99% HB	No	No	1	Cystic	Oper.	0	
3. F. R.	F	46	W	Yes 5,660,000 RBC 112% HB	No	No	2	Cystic	Oper.	0	Psychiatric symptoms prominent; ventriculogram elsewhere 1 month previously was normal
4. C. L.	M	36	C	No 5,280,000 RBC 15.6 gms HB	Yes (OS)	No	1	Solid	Oper.	0	Postoperative radiation therapy
5. J. E.	M	34	W	No	No	No	2	Cystic	Oper.	0	Psychiatric treatment (shock therapy) after second operation for depression
6. M. S.	F	22	W	No	No	No	1	Cystic	Oper.	0	
7. L. V.	M	44	C	No	Retinal hemorrhage	No	1	Cystic	Oper.	Yes	Positive Wassermann: ? coronary occlusion 3 weeks after operation; no postmortem

8. L. W.	M	44	W	No 5,300,000 RBC	No	See remarks	2	Cystic	Oper.	0	Five close relatives died of "headaches"
9. L. L.	M	20	W	Died before laboratory work done	No	No	0	Solid	P.M.	0	Died one hour after onset of symptoms of massive cerebellar hemorrhage
10. A. H.	F	55	W	Yes 5,190,000 RBC 98% HB	No	No	0	Cystic	P.M.	0	Also had pheochromocytoma of adrenal and cutaneous Von Recklinghausen's disease
11. H. R.	M	40	W	Yes 8,070,000 RBC 22.5 gms HB	No	No	3	Cystic	Oper.	0	Postoperative radiation therapy. Three operations in seven years. Excellent condition 10 yrs later
12. M. B.	F	61	W	Yes 136.8% HB 21.9 gms % HB	No	No	1	Cystic	Oper.	0	
13. I. D.	F	60	W	No	No	No	1	Cystic	Oper.	0	
14. M. H.	F	19	W	No	No	No	2	Cystic	Oper.	Yes	Benign papilloma of right ovary found at postmortem

disks (56 per cent) although practically all of these patients were alert on admission. The average duration of symptoms before admission was 10 months. In 5 cases a history of head injury previous to the development of acute symptomatology was considered of possible etiologic significance in the Lahey Clinic series. Percival Bailey[1] had seen only one example of Lindau's syndrome up to 1948 although hemangiomatous tumor of the cerebellum is not very rare.

SYMPTOMS AND SIGNS

The general signs of increased intracranial pressure are usually present in these cases. These are (1) headache, (2) vomiting—often projectile, (3) choked disks. The localizing signs of cerebellar disease consist chiefly of marked nystagmus, ataxia, which may be unilateral, a positive Romberg sign, adiadokokinesia, hypotonia and suboccipital tenderness to firm pressure.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of cerebellar hemangioma is always suggested by the development of such symptoms and signs (just described) in an individual in the 22 to 45 year old or even older age group. The only other important posterior fossa lesion to rule out in this age group is ependymoma of the cerebellum. Such a lesion was disclosed in a 53 year old white man in our clinic recently. The acoustic tumor, which has a quite different symptomatology, must also be ruled out. Lastly, metastatic malignant cerebellar disease, not a rare complication of otherwise *silent* carcinoma of the lung and kidney particularly must always be thought of in the middle and later decades of life. Medulloblastoma cerebelli in an adult is very rare although a 36 year old patient was operated upon (August 1953) at our clinic with successful outcome. The retinae should be scrutinized very carefully through dilated pupils. Often the characteristic angioma of the retina (von Hippel's disease) is obscured by a retinitis, detached retina or other ocular pathology (see above). Skull roentgenograms and other laboratory data are usually of little or no value in identifying these tumors preoperatively except that occasionally an erythrocytosis is demonstrated.

ERYTHROCYTOSIS IN THESE LESIONS

Considerable discussion has appeared in the literature concerning whether or not these tumors may cause, or be associated with, erythrocytosis. We prefer the term *erythrocytosis* rather than *polycythemia* as the latter term suggests neoplastic formation of erythrocytes in the bone marrow. Erythrocytosis occurred in 6 of our 14 cases (42.9 per cent). Earl Walker[26, 16] stated in 1950 that in a series of 52 cerebellar hemangioblastomas verified at the Johns Hopkins Hospital, the incidence of erythrocytosis was 20 per cent. Several cases now are on record[4] in which removal of the hemangiomatous cerebellar nodule in patients with erythrocytosis resulted in recession of the elevated erythrocyte count to normal. Such a case also is reported by Woolsey[27] of St. Louis (1951).

Johnson and Chalgren[15] (1951), point out that at least 2 cases of *polycythemia* in pituitary basophilism are on record, one of the patients having a basophilic

adenoma, while the other had a suprarenal tumor. They quoted Barker and Craig who reported 2 cases in which polycythemia was associated with tumors in the region of the third ventricle. Drew and Grant[12] collected 10 cases including *sarcoma* of the convexity of the left frontal lobe, glioblastoma of the right parietal lobe and endothelioma of the right frontal region, all associated with *polycythemia*. They included 1 of their own cases: a patient with a large chronic subdural hematoma who also had erythrocytosis which receded after drainage of the clot, but the erythrocytosis recurred five months later. Oppenheim referred to a case of polycythemia in which a cerebellar medulloblastoma was found at autopsy.

The common factor in all of these cases of tumor in areas of the brain other than the diencephalon was a *marked increase in cerebrospinal fluid pressure*. It is possible that this increased pressure might have been transmitted from the third ventricle to the neighboring hypothalamic centers which, in turn, influence water metabolism and/or erythropoietic activity. It is believed that there is a center for stimulation of the formation of erythrocytes in the diencephalon. As all the cerebellar hemangiomas that come to operation have internal hydrocephalus of greater or lesser degree, this latter theory seems more plausible than that there is any inherent erythropoietic function *per se* in these interesting hemangiomatous tumors, especially as thorough microscopic study of our pathologic material in 14 cases fails to reveal any areas in these tumors of structures that could truly be called hematopoietic; nor is the tumor tissue in these cases ever found to be embryonal. It is always *adult* tissue, therefore, *the term "hemangioblastoma", in the opinion of the authors, is a misnomer*. Cramer and Kimsey[6] submitted a portion of one of these tumors to Dr. Margaret Murray of Columbia University who tried tissue culture technic. Most of the erythrocytes arising from the growth of the tumor were of the size of normal red cells, but in other areas they were larger and resembled erythroblasts. It was concluded that this single tissue growth experiment with only one of these tumors was not conclusive as to the presence or absence of erythropoietic capacity in these hemangiomas.

On the other hand, Silver and Hennigar[23] (1952) found in all but one of their cases, no histologic evidence that there was any hematopoiesis within the tumor itself after extensive microscopic study of 40 tumors. Turner and Kernohan[25] (1941) stated that there was no proof of hematopoiesis in their cases. However, Woolsey's[27] clinical report (1951) is very convincing with respect to the tumor nodule, that developed later in his patient, having possible erythropoietic properties.

OPERATIVE FINDINGS AND GROSS PATHOLOGY

The operations are invariably done today in our clinic under intratracheal ether or gas-oxygen anesthesia. A bilateral approach is made to the cerebellum, either via a mastoid to mastoid incision or by a vertical midline exposure. The dura is widely opened after the occipital sinus has been occluded. Often the cystic lesion is discernible by a certain fullness, flattening or discoloration of the

cerebellar surface or there may be an angiomatous tuft of vessels present on the posterior cerebellar surface. Cautiously tapping the suspected hemisphere with a ventricular needle will verify a subsurface cystic lesion. Percival Bailey[1] and and other writers[18, 8, 22] have long recognized two chief types of lesions grossly: (1) a solid angiomatous mass without cystic component usually situated in the midline at the posterior end of the fourth ventricle and (2) the better known and more frequently described *cystic* hemangioma with a mural nodule in one or the other cerebellar hemispheres or even in the vermis (figs. 1, 2, 3). The nodule is best removed with the aid of the electrocautery—since 1928—the biopsy forceps or, occasionally, it may be dissected out en masse with a brain or pituitary spoon.

When the angiomatous nodule is removed in the cystic cases, an early and permanent cure should result. The cyst may contain only semisolid gelatinous material; the solid mural angioma appearing in the cyst at a later operation that may be necessitated by a recurrence of symptoms. Prior to the 1920's or certainly the second decade of the twentieth century, most of these cases were pathologic curiosities only and were doomed eventually to a fatal outcome, usually without operation. Buck and Steer[3] quote Hughlings Jackson (1872) as recording a fatal lesion of this type. Other writers of the latter part of the nineteenth century—quoted by Perlmutter et al[22]—recorded and clearly described similar lesions. With the advent of electrosurgery in 1928 the excision of the mural nodule in cystic cerebellar lesions of all types became practically routine.

The solid cerebellar hemangiomas without cystic component are often best left in situ and irradiated postoperatively through a wide cerebellar decompression. Occasionally a solid hemangioma of the cerebellum will manifest itself clinically with a catastrophic onset which may terminate fatally and is verified at postmortem examination. Such was the case with one of our patients (case no. 9). An apoplexy-like onset and fatal termination from a similar lesion of the cerebellum, first demonstrated at postmortem examination, occurred in a young student nurse some years ago in one of the Richmond hospitals. The gross

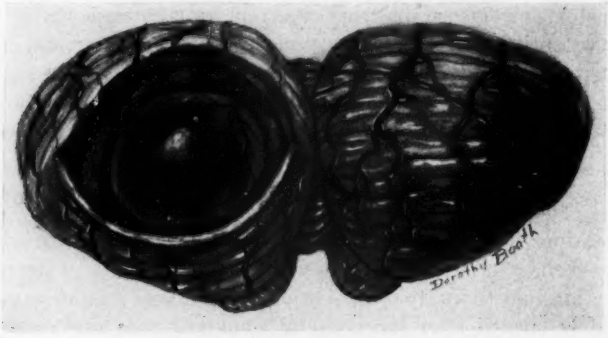


FIG. 1. Thirty-four year old man (two operations); artist's drawing of left cerebellar cyst containing angiomatous tuft and a gelatinous jelly-like mass (case no. 5—table I).

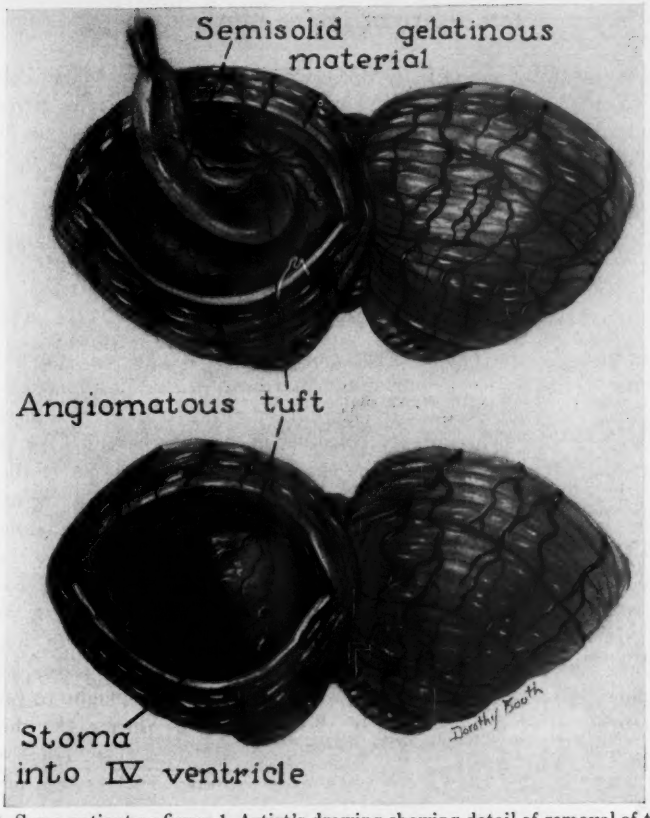


FIG. 2. Same patient as figure 1. Artist's drawing showing detail of removal of the gelatinous mass: the angiomatous tuft was coagulated and a stoma made between the cyst and the underlying fourth ventricle. No recurrence of symptoms 14 months after second and last operation.

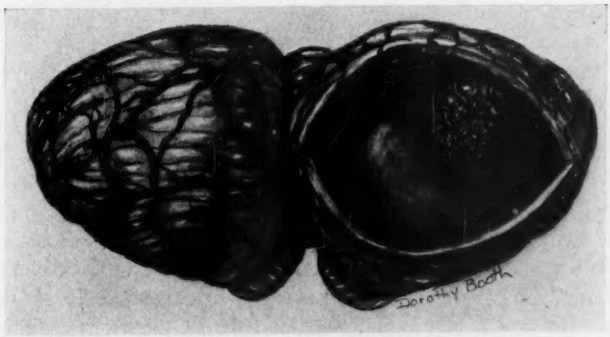


FIG. 3. Forty year old man (three operations). Diagrammatic drawing showing large vascular mural nodule in right cerebellar cyst which was removed piecemeal by electrocoagulation at third operation. Symptom free and working regularly but erythrocytosis still present 10 years after last operation, (case no. 11—table I), in spite of phlebotomies and radioactive phosphorus therapy.

specimen was seen by one of us (JMM). Cramer and Kimsey[6] cite Globus and also Wedd, each of whom reported cases of spontaneous hemorrhage from cerebellar hemangiomas. Bailey[1] reports a surgical attack on such a case in which removing a small portion of tissue for biopsy almost exsanguinated the patient on the table, but the hemorrhage was eventually controlled. A similar experience occurred with one of our own cases in 1938. With present-day efficient methods of hemostasis, the necessity for multiple operations in the future should be less frequent.

EMBRYOLOGY

Percival Bailey[1] stated (1948) that the origin of these tumors is from a vascular primordium at the posterior end of the fourth ventricle. He describes embryologically—in the angle between the cerebellum and the brain stem in the third fetal month—a very rich capillary plexus of blood vessels which for the most part enters into the formation of the choroid plexus in the roof of the fourth ventricle. A smaller portion forms a vascular tangle at the posterior extremity of the fourth ventricle. In this latter vascular anlage these hemangiomas may be located, particularly the solid growths, although they may also be found over the lateral surfaces of the cerebellar hemispheres or even in or on the spinal cord—such as case 3, reported by Craig and Horrax[5]—where they may possibly arise in relation to similar vascular primordia. The reason for the association of these various pathologic alterations—brain, spinal cord, retina, pancreas, liver, kidney, epididymis—is not entirely clear but it is thought to be due to some disturbance of development of the mesenchyme during the third fetal month. One of our cases—case no. 10—was of interest in this connection. A 55 year old white woman had (1) typical von Recklinghausen's disease proved by biopsy of a skin lesion, (2) a cystic hemangioma of the cerebellum and (3) a large pheochromocytoma of the left adrenal gland—all three lesions being illustrative of a primary mesenchymal disorder. Similarly, Lowenthal[20] (1950) recorded the case of a 43 year old man with a "cerebellar hemangioblastoma, an entirely separate meningeal hemangioblastoma in the left parieto-occipital area with bony metaplasia, together with hypertrophy of the choroid plexus—mass the size of an olive in a lateral ventricle—and amorphous calcium deposits in the plexus."

HISTOLOGY

The essential lesion of angiomatosis retinae—von Hippel's disease—has been shown to be a capillary hemangioma. The hemangioma of the retina may be microscopic in size and therefore not seen at all by ordinary ophthalmoscopic examination even through dilated pupils. Poppen believes the retinal lesion and the cerebellar lesion usually are on the same side. Lichenstein[17] states that often it is difficult microscopically to differentiate between primary cerebellar hemangioma and metastatic hypernephroma.

Histologically, cerebellar hemangioma may be classed into three types: (1) *Juvenile* (2) *Transitional* and (3) *Clear Cell Types.*[23]

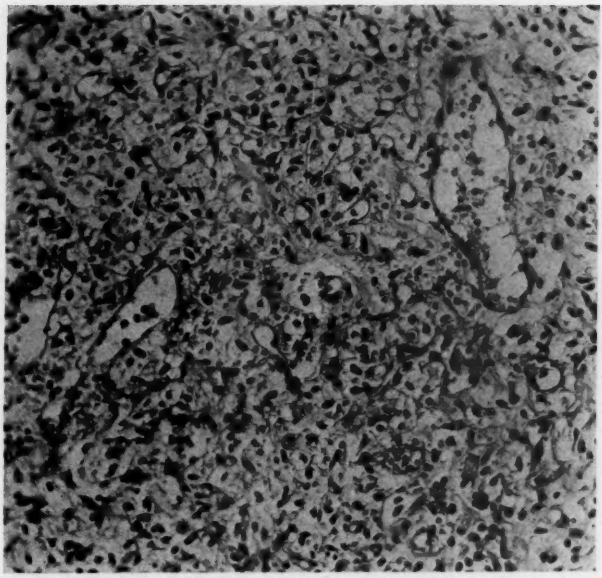


FIG. 4. *Juvenile* type. A mixture of small and large capillaries is seen (capillary-cavernous hemangioma) H and E × 200.

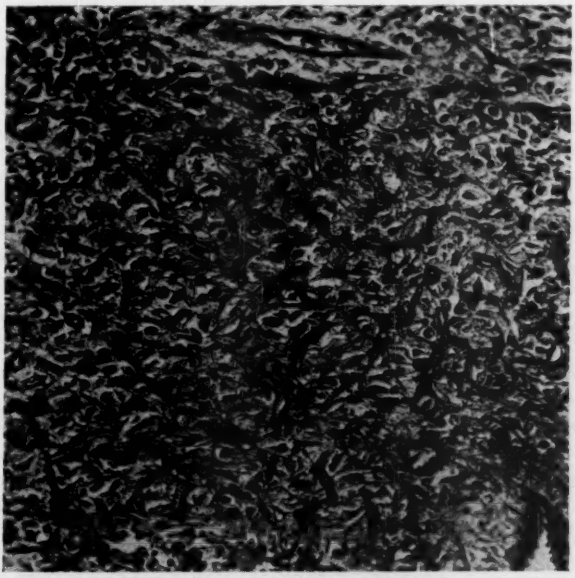


FIG. 5. *Juvenile* type. Numerous small capillaries and abundant endothelial cells (capillary hemangioma) H and E 300.

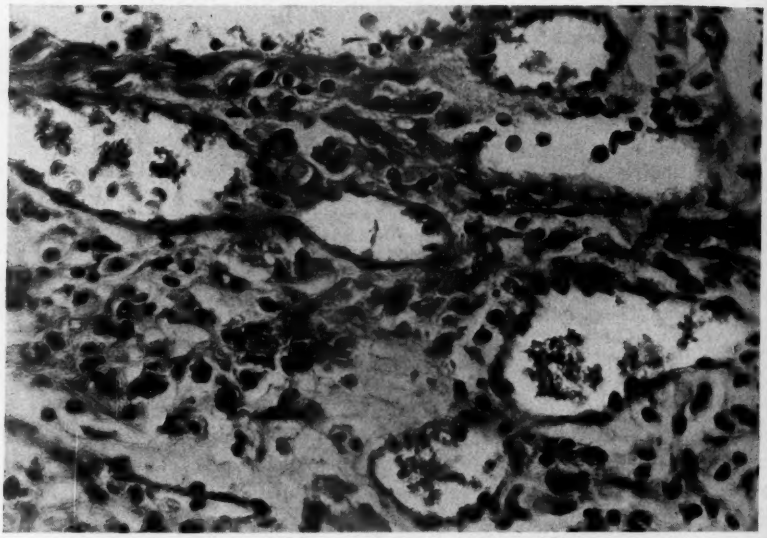


FIG. 6. *Juvenile* type. Large dilated capillaries lined by single layer of endothelial cells are evident. Between the capillaries are scattered endothelial cells (cavernous hemangioma) H and E × 400.

(1) The *juvenile* type (fig. 4) is characterized by sheaths of capillaries of small size lying adjacent to one another in a uniform pattern. Endothelial cells are abundant throughout the stroma of the tumor. This type of hemangioma is not only seen in the cerebellum but may be found in other tissues. For example, hemangiomas in the scalp of the newborn infant may duplicate the structure described above and be confused with malignancy by the inexperienced pathologist because of the marked endothelial cellularity (fig. 5). Possibly this microscopic picture may have induced previous workers to refer to this neoplasm as hemangioblastoma. One frequently finds intermingled with the tiny capillaries, larger dilated or prominent vessels as seen in figure 6. In other words, the juvenile type *histologically* is a capillary-cavernous hemangioma. *Clinically*, hemangioma is a malformation which we believe is present at birth and usually lies dormant until the close of the second decade of life or later when a change occurs either in the tissue itself or its surroundings. Then clinical symptoms and signs develop. It would appear that the malformation is undergoing neoplastic change at that time and, in the case of the cystic tumors, either hemorrhagic degeneration or excessive secretion of serum resulting in the formation of the cysts has occurred.

(2) The *transitional* type has recently been characterized[23] as "A transition from the juvenile to the clear cell type of hemangioma. The cytoplasm becomes more clear staining and a few to moderate number of large multinucleated giant cells appear; microcysts become prominent and there are areas of hemorrhage. Thus the uniform appearance of the juvenile type is lost." It might be added that from the study of our present material of 14 cases that the cytoplasm becomes not only more abundant, lighter or clearer-staining in this type, but

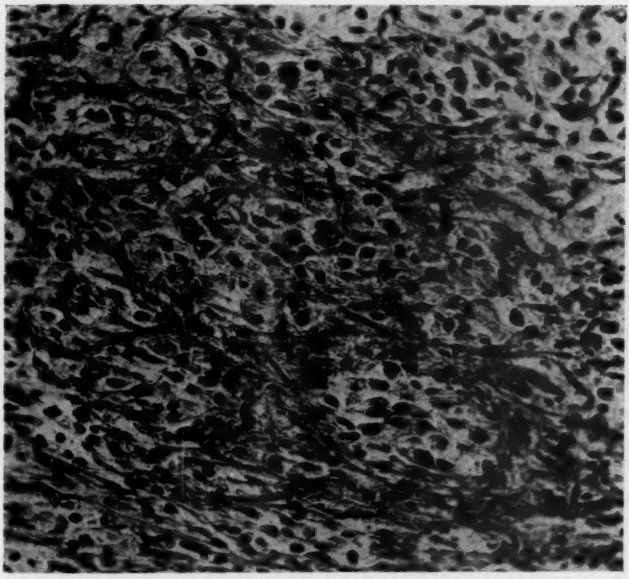


FIG. 7. *Transitional* type. Endothelial cells with bright staining, finely granular cytoplasm and a few large bizarre-appearing mononuclear cells. H and E × 300.

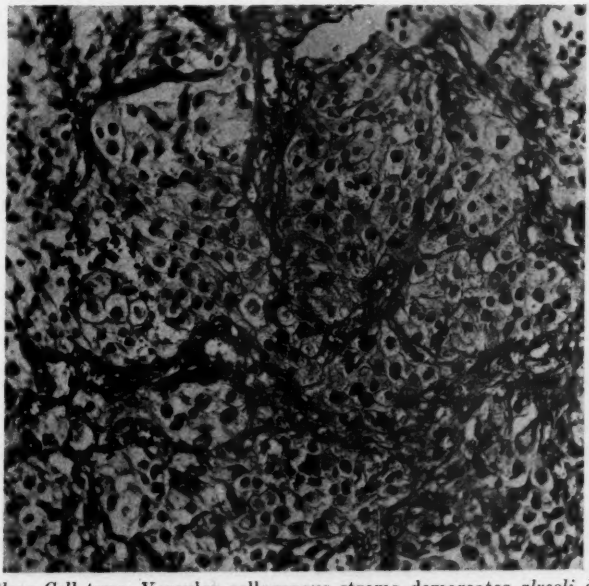


FIG. 8. *Clear Cell* type. Vascular collagenous stroma demarcates *alveoli* composed of clear-staining endothelial (xanthoma) cells. Variation in size, shape and staining properties of the nuclei is seen. H and E × 300.

also finely granular large mononuclear cells, frequently rich in chromatin, were evident (fig. 7).

(3) The *clear cell* type is characterized by alveolar formations composed of large cells containing voluminous clear staining cytoplasm which is Sudanophilic and may be considered as xanthoma cells (fig. 8). It has been proposed (Silver and Hennigar)[23] that hemorrhage occurring within the tumor liberates fatty materials which are phagocytized by endothelial cells of the neoplasm which then are referred to as xanthoma cells. In this series of cases the clear cell type of tumor was found only in the older age group. Correlation between the histopathology and the age of the lesion (patient) as previously reported (Silver and Hennigar[23]) is corrobated by this present study.

SUMMARY

On the whole, the cerebellar hemangiomas, particularly the cystic ones with a mural nodule, are much more favorable lesions than the gliomatous growths, cystic or solid, that occur even more frequently in the cerebellum at a considerably earlier age, although surgical treatment of the astrocytomatous cerebellar cysts with a mural nodule in children has long been one of the triumphs of modern neurosurgery. The cystic lesions described in this paper seem to respond well to reoperation if necessary. Irradiation is also of distinct value postoperatively if they cannot safely be completely removed (as in the large solid hemangiomas at the caudal end of the fourth ventricle). These lesions are all benign histologically; malignancy in hemangioma cerebelli is almost unheard of in this or any location in the body.

A clinico-pathologic study of 14 cases of cerebellar hemangioma from our clinic is presented with special emphasis on their symptoms and signs, methods of diagnosis and differential diagnosis of the lesion, and a consideration of whether there is a more than coincidental erythrocytosis associated with these tumors. The operative findings, the types of gross pathology, the three histological variations and the embryology of these interesting lesions are also described. A brief discussion is made with reference to the occasional occurrence of a retinal angioma in these cases and the familial incidence of hemangiomas of the central nervous system is considered.

The designation "hemangioma" rather than "hemangioblastoma"—the more frequently used pathologic term—is preferred for reasons given in the body of the paper.

N.B. Since this paper was first prepared for publication we have encountered (August, 1953) an additional (15th) case of this lesion. The symptoms were rapidly progressive, terminating in death. A 24-year-old white woman, 8½ months pregnant, developed sudden headache and became comatose in a few hours. She was admitted to the hospital and spinal puncture three hours after onset of symptoms showed quite bloody spinal fluid. The patient died six hours after onset of symptoms, presumably of a massive spontaneous subarachnoid hemorrhage. At post-mortem examination, three hemangiomatous nodules were found arising on the posterior and lateral surfaces of the medulla, from which had come the fatal subarachnoid hemorrhage.

Note. The attending and resident neurosurgeons at the Medical College of Virginia who operated upon the 12 surgical cases reported in this paper (table I) were as follows: Drs. C. C. Coleman, W. G. Crutchfield, J. M. Meredith, George Gish, Jr., and Robert Waters. Case no. 11 was operated upon by Dr. E. P. Lehman of the University of Virginia Hospital, Charlottesville, in 1935.

REFERENCES

1. Bailey, P.: Intracranial Tumors, ed. 2, Springfield, Ill., Charles C. Thomas, 1948, p. 185.
2. Bailey, P.; Buchanan, D. N., and Bucy, P. C.: Intracranial Tumors of Infancy and Childhood, Chicago, University of Chicago Press, 1939.
3. Buck, C. E., and Steer, A.: Hemangioblastoma of central nervous system, U. S. Armed Forces J. M. *3:* 907 (June) 1952.
4. Carpenter, G.; Schwartz, H. G., and Walker, A. E.: Neurogenic polycythemia, Ann. Int. Med. *19:* 470 (Sept.) 1943.
5. Craig, W. McK., and Horrax, G.: Occurrence of hemangioblastomas (two cerebellar and one spinal) in three members of family, J. Neurosurg. *6:* 518 (Nov.) 1949.
6. Cramer, F., and Kimsey, M. W.: Cerebellar hemangioblastomas; review of fifty-three cases, with special reference to cerebellar cysts and association of polycythemia, A.M.A. Arch. Neurol. & Psychiat. *67:* 237 (Feb.) 1952.
7. Cushing, H. W.: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, 1932, p. 119.
8. Cushing, H. W., and Bailey, P.: Tumors Arising from the Blood Vessels of the Brain; Angiomatous Malformations and Hemangioblastomas, Springfield, Ill., Charles C. Thomas, 1928.
9. Dandy, W. E.: Venous abnormalities and angiomas of brain, Arch. Surg. *17:* 715 (Nov.) 1928.
10. Danis, P.: Aspects ophthalmologiques des angiomatoses du système nerveux, Acta neurol. et psychiat. belg. *50:* 615 (Nov.) 1950.
11. Davis, L., cited by Perlmutter, I. et al.[22]
12. Drew, J. H., and Grant, F. C.: Polycythemia as neurosurgical problem: review, with reports of two cases, Arch. Neurol. & Psychiat. *54:* 25 (July) 1945.
13. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, ed. 2, Springfield, Ill., Charles C. Thomas, 1944, p. 789.
14. Hicks, S. P., and Warren, S.: Introduction to Neuropathology, New York, McGraw-Hill Book Company, Inc., 1950, p. 374.
15. Johnson, D. R., and Chalgren, W. S.: Polycythemia vera and the nervous system, Neurology *1:* 53 (Jan.–Feb.) 1951.
16. Lichtenstein, B. W.: Lindau's disease—pathological observations, J. Neuropath. & Exper. Neurol. *10:* 103 (Jan.) 1951.
17. Lichtenstein, B. W.: Hemangioblastoma and Lindau's disease, Arch. Neurol. & Psychiat. *65:* 406 (March) 1951.
18. Lichteinstein, B. W.: A Textbook of Neuropathology, Philadelphia, W. B. Saunders Company, 1949, p. 292.
19. Lindau, A.: Studien über Kleinhirncysten; Bau, Pathogenese und Beziehungen zur Angiomatosis Retinae, Acta path. et microbiol. Scandinav. (Supp. no. 1) 1926, p. 1.
20. Löwenthal, A.: Cerebellar hemangioblastoma, meningeal hemangioblastoma with bony metaplasia, hypertrophy of choroid plexus with amorphous calcium deposits in same patient, Acta neurol. et psychiat. belg. *50:* 185 (April) 1950.
21. Olivecrona, H.: Cerebellar angioreticulomas, J. Neurosurg. *9:* 317 (July) 1952.
22. Perlmutter, I.; Horrax, G., and Poppen, J. L.: Cystic hemangioblastomas of cerebellum; end results in twenty-five verified cases, Surg., Gynec. & Obst. *91:* 89 (July) 1950.
23. Silver, M. L., and Hennigar, G.: Cerebellar hemangioma (hemangioblastoma); clinicopathological review of forty cases, J. Neurosurg. *9:* 484 (Sept.) 1952.
24. Tonning, H. O.; Warren, R. F., and Barrie, H. J.: Familial hemangiomata of cerebellum; report of three cases in family of four, J. Neurosurg. *9:* 124 (March) 1952.
25. Turner, O. S., and Kernohan, J. W.: Vascular malformations and vascular tumors involving spinal cord; pathologic study of forty-six cases, Arch. Neurol. & Psychiat. *46:* 444 (Sept.) 1941.
26. Walker, A. E., in discussion on Lichtenstein, B.W.[16]
27. Woolsey, R. D.: Hemangioblastoma of cerebellum with polycythemia; case report, J. Neurosurg *8:* 447 (July) 1951.

THE EARLY DIAGNOSIS OF CARCINOMA OF THE ESOPHAGUS*

EDWARD F. PARKER, M.D.

Charleston, S. C.

Carcinoma of the esophagus is still a highly malignant and rapidly fatal disease despite encouraging reports appearing in the literature from time to time concerning its successful treatment. Its seriousness may be contrasted with that of malignant melanoma, a tumor generally considered to be very highly malignant, in which Pack[4] reported that the five year survival rate was approximately 21 per cent. In cases of carcinoma of the mid-thoracic esophagus treated by resection, Sweet[6] has reported that the survival rate of five years or greater was 0.9 per cent (1 of 107 cases). Gibbon and associates[3] have recorded a three and one-half year survival rate of zero in 63 cases of primary carcinoma of the esophagus. The writer and associates[5] have reported a three year survival rate of 0.6 per cent (1 case) in 170 cases of primary carcinoma of the esophagus.

There is little doubt that the chance for survival in cases of carcinoma of the esophagus has been increased as a result of the introduction by Adams and Phemister,[1] and Churchill and Sweet,[2] of the principles involved in its successful extirpation combined with restoration of the continuity of the alimentary tract in a single stage operation. Even so the results of the surgical treatment are obviously exceedingly poor. However, it should be pointed out that until the patients with this disease have the advantage of diagnosis and treatment before it has reached a far-advanced stage, the potentialities of success in the surgical treatment of this disease have not begun to be realized.

In order to obtain improvement in the results of the surgical treatment, primary emphasis must be laid upon earlier diagnosis. Patients afflicted with carcinoma of the esophagus too frequently have in common with patients afflicted with malignant tumors of other internal viscera and tissues, the tremendous disadvantage of not having access to surgical treatment until the disease is far-advanced. The patient with carcinoma of the esophagus is at an even greater disadvantage because of the rapidly increasing starvation to which he is peculiarly subject after mechanical obstruction of the lumen develops.

While not always adequate by any means, there are available at present methods of study, the use of which could lead to the establishment of the diagnosis much earlier in many cases. A study of our cases has made it clear that the reason for late diagnosis in the majority is not the failure of the patient to consult a physician soon after the onset of symptoms, but rather that the physician often does not interpret the symptoms as indicating the possibility of carcinoma of the esophagus and therefore does not institute the proper diagnostic procedures as soon as possible.

In order to ascertain the reasons for delayed diagnosis in many cases, we have

* From the Cancer Clinic of the Medical College of South Carolina and the Roper Hospital.

reviewed the records of 187 cases of primary epidermoid carcinoma—all proved histologically—seen in the Cancer Clinic of the Medical College of South Carolina and in the Roper Hospital between January 1940 and March 1951. It was considered that the diagnosis was established about as early as possible in 69 patients who had had symptoms of two months or less duration. In the remaining 118 patients, most of whom had symptoms of longer duration, there were 17 patients (14.4 per cent) in whom there was a significant delay in establishing the diagnosis, for reasons other than the usual lack of suspicion.

The symptoms most commonly associated with carcinoma of the esophagus were as follows—in order of frequency: dysphagia (a sense of obstruction), weight loss, pain on swallowing, regurgitation of food, cough, hoarseness, substernal fullness, nausea and vomiting, hematemesis, hemoptysis, fever, singultus, sore throat, dyspnoea, and melena. Dysphagia was the first symptom in the majority, occurring in about 70 per cent of the patients. In the remaining patients, pain on swallowing was most commonly the first symptom. Except for evidence of loss in weight and strength, physical signs of carcinoma of the esophagus were notoriously lacking in the absence of direct extension of the tumor beyond the esophagus or of distant metastasis.

The erroneous diagnoses entertained before carcinoma of the esophagus was suspected were the following: carcinoma of the stomach, peptic ulcer, cardiospasm, gastric neurosis, esophageal varices, cholecystic disease, coronary disease, aneurysm of the aorta, and cervical or intrathoracic goitre.

There are two examinations indicated in any patient having any of the above symptoms, or any other symptom which might possibly be construed as indicating an alteration in esophageal function. These are radiographic study of the esophagus using barium or lipiodol, including both fluoroscopy and roentgenographic films, and esophagoscopy. The latter should be used even if the radiographic studies are normal.

Since 90 per cent of patients with carcinoma of the esophagus have dysphagia and a filling defect in the esophagus upon radiographic examination, it is to be expected that delays in the completion of adequate studies, and therefore in establishing the correct diagnosis, would be encountered most frequently in those patients not presenting either or both of the above features. Actually, in our series of cases, delays in diagnosis for reasons other than lack of suspicion were encountered in the following groups of patients:

1. Those having no dysphagia.
2. Those having no dysphagia but having an abnormal esophagogram, in whom carcinoma was not suspected because of absence of complaints on swallowing.
3. Those having spontaneous but temporary cessation of dysphagia.
4. Those having dysphagia but no roentgenographic evidence of obstruction.
5. Those having roetngenographic evidence of an abnormality interpreted erroneously as being due to esophageal disease other than carcinoma—such as esophageal varices—in whom a single esophagoscopic examination was normal.
6. Those having other readily demonstrable physical defects invoked errone-

ously as the cause of symptoms referable to swallowing—such as cervical goitre.

7. Those in whom exploratory operation may have been necessary in order to establish the diagnosis.

There follow case reports illustrating the difficulties in the diagnosis of carcinoma in each of the above groups. It will be noted that several of the cases fall into more than one of the above groups.

Case 1. I. W., a white man, aged 46, was admitted to the hospital in September 1947, because of sore throat, burning in the throat on swallowing, chronic alcoholism, malnutrition, pellagra and anemia. The clinical impression was that the dysphagia was due to so-called sideropenic dysphagia. Roentgenograms of the esophagus revealed a mild dilatation in the lower portion. On esophagoscopy, the findings were normal except for evidence of leukoplakia in the thoracic esophagus. Tissue for biopsy was taken at random at a level 30 cm. beyond the alveolar margin. The biopsy revealed epidermoid carcinoma in the submucosa. Esophagoscopy was repeated. The site where tissue for biopsy was removed was not recognizable. There was no abnormality except leukoplakia. Tissue for another biopsy taken at the 30 cm. level showed only esophagitis. Roentgenographic studies of the esophagus were repeated and were normal. On laryngoscopy, a large ulcer of the epiglottis was found. Biopsy of this ulcer revealed epidermoid carcinoma. The carcinoma of the esophagus was considered inoperable at the time because of severe malnutrition. A gastrostomy was done. Roentgen ray therapy was given over the larynx. On a third esophagoscopy there was found a polypoid-like mass at the 35 cm. level. A biopsy showed epidermoid carcinoma.

The sore throat and pain on swallowing disappeared after radiation treatment of the epiglottis. In January 1948, on a fourth esophagoscopy, there was no evidence of carcinoma. On this examination a papilloma was found at the base of the tongue; biopsy of this revealed epidermoid carcinoma. He became able to eat any food. He used the gastrostomy practically not at all and gained 10 lbs. On esophagoscopic examination in February 1948, epidermoid carcinoma with very slight narrowing was found at the 37 cm. level proved by biopsy. He continued to swallow well until April 1948, when a sense of obstruction opposite the xiphoid developed. In May 1948, roentgenograms of the esophagus revealed an irregular constriction at the level of the eighth thoracic vertebra. Thereafter he had progressively increasing dysphagia and died in August 1948. At autopsy, residual carcinoma of the epiglottis was present. There was only one carcinoma found in the esophagus, 5 cm. beyond the level of the carina, with no extension beyond the esophagus.

Comment: The above case represents one in whom the initial dysphagia was due to an ulcerating carcinoma of the epiglottis. The carcinoma of the esophagus was found accidentally and produced no dysphagia for seven months after it was first discovered. For the same reason that the lesion was not large enough to result in any diminution in the size of the lumen when first discovered, it was also not large enough to produce any abnormality on radiographic examination of the esophagus.

Case 2. W. D. V., a white man, aged 72, was admitted to the hospital in January 1952, because of massive hematemeses, weakness, dizziness and loss in weight. He had no pain or obstruction on swallowing. The past history and the physical examination were noncontributory. Fluoroscopic studies of the upper alimentary tract revealed no abnormality in the esophagus, stomach or duodenum. Although no abnormality was seen on fluoroscopy, roentgenographic films of the thoracic esophagus were made because varices—but not carcinoma—were suspected. The films showed an irregularity in one area (fig. 1). On the day after admission he had a convulsion and a change in speech. Thereafter he presented evidence of persistent intracranial disease and was in a semicoma most of the time. Esophagoscopy was done a week later and there was found a concentric narrowing 37 cm. beyond the alveolar margin. A biopsy of tissue taken at this site revealed normal mucosa. He died in February 1952, of complications due to perforation of the esophagus. Autopsy

FIG. 1

FIG. 2

FIG. 1. Case 2. Photograph of an esophagogram. The arrow points to an irregular filling defect not noticed during the fluoroscopic examination. The lumen was normal in size. At autopsy, carcinoma of the esophagus was found.

FIG. 2. Case 2. Photograph of fixed specimen. The esophagogastric junction is at the bottom. The esophagus has been opened through the carcinoma, represented by a large shallow ulcer. Three blocks of tissue have been removed from the half of the ulcer on the right side. There was no diminution in the size of the lumen.

revealed epidermoid carcinoma of the esophagus without any diminution in the size of the lumen (fig. 2).

Comment: The above case is cited to show that carcinoma of the esophagus may exist without producing narrowing of the lumen and without causing dysphagia. Also it is apparent that a large ulcer of the esophagus can be present without any abnormality being detectable on fluoroscopic examination. Therefore, in known or suspected disease of the esophagus, roentgenographic films should be made in addition to the fluoroscopic observations.

Case 3. J. R., a Negro man, aged 54, was seen in November 1950, complaining of pain in the stomach and substernal region of three days duration, with a sensation of food *sticking* while going down. Radiographic studies of the esophagus were normal. Thereafter his symptoms disappeared until April 1951. This was ascertained in May 1951, on admission to the hospital because of progressive dysphagia of two months duration, with 45 lbs. loss in weight, occasional tarry stools and occasional vomiting of blood. Radiographic studies of the esophagus revealed a lesion in the middle third of the thoracic esophagus. On esophagoscopy there was an obstructing ulcerating lesion 31 cm. beyond the alveolar margin. A biopsy revealed epidermoid carcinoma. Esophageal resection with intrathoracic esophagogastric anastomosis was done. His initial progress was satisfactory and he was swallowing well. However, later the anstomosis disrupted. This was followed by empyema and death.

Comment: In the above case, it is reasonable to believe that the symptoms manifested first in November 1950, were due to carcinoma of the esophagus. Esophagoscopy on one or more occasions should have been done at that time because of the possibility of carcinoma, even though the radiographic studies were normal.

Case 4. E. J., a Negro man, aged 45, was admitted to the hospital in May 1947, because of difficulty in swallowing and burning in the chest of one month duration. There was also pain in the epigastric region aggravated by eating. He had lost 35 lbs. in weight in the previous two years. The physical examination was normal except for the presence of a hard supraclavicular node on the left. The clinical impression was that of carcinoma of the esophagus with cervical lymph node metastasis. Radiographic studies of the esophagus were normal. This was followed by esophagoscopy which revealed a small polypoid friable lesion 20 cm. beyond the alveolar margin. The biopsy revealed epidermoid carcinoma. Further radiographic studies of the esophagus were normal. The cervical lymph node was removed and found to contain epidermoid carcinoma. The esophageal lesion was considered to be incurable and a gastrostomy was done. He had a progressively downhill course and died in September 1947, six months after the onset of dysphagia.

Case 5. R. T., a Negro woman, aged 66, was observed in the clinic in November 1948, complaining of "my stomach crawls and I have pains in the stomach." The symptoms were of about three months duration. The pain was very severe and continuous. The physical examination was not remarkable except for the presence of a cervical goitre. Radiographic studies of the upper alimentary tract were normal except for a kink in the distal esophagus. Roentgenograms of the chest revealed evidence of a substernal goitre. She was not seen again until January 1949, with the same complaints. Esophagoscopy was advised but she did not return until one month later. Esophagoscopy was done and no abnormality was noted in the lower esophagus. On withdrawing the scope there was found a 1 cm. ulcer on the anterior wall of the esophagus 22 cm. from the alveolar margin. A biopsy revealed epidermoid carcinoma. There was no obstruction. She absented herself until April 1949, when she complained of weakness, fever, rheumatism, *heatness* beneath the lower end of the sternum and burning on swallowing hot foods, but she had no sense of obstruction on swallowing. Radiographic studies of the esophagus were normal (fig. 3). A thyroidectomy was done following which she made an uneventful recovery. Two weeks later, an esophagectomy was done with restoration of continuity by an intracervical esophagogastrostomy. The carcinoma was situated (fig. 4) opposite the arch of the aorta. Again microscopic sections revealed epidermoid carcinoma. Her recovery was uneventful, but she died in September 1950, after the appearance of metastatic nodes in the neck.

Comment: The last 2 cases represent excellent examples of carcinoma of the esophagus in whom the lesions were not large enough to produce filling defects upon careful radiographic examinations, even after the radiologist was informed of the presence of carcinoma proved by biopsy. It has been our experience that unless a lesion of the esophagus involves a third or more of the circumference, its presence may be exceedingly difficult to detect upon radiographic examination. Hence it is obvious that a normal radiographic study of the esophagus does not exclude the presence of a small lesion, and that esophagoscopy is indicated in the study of any patient with suspected esophageal disease, regardless of the result of the radiographic studies.

Case 6. W. D. P., a Negro man, aged 46, was admitted to the hospital in March 1945, with the complaints of stomach trouble, weakness, anorexia and weight loss of eight months duration. He also had frequent vomiting after meals, substernal and epigastric pain and more recently small hematemeses and hoarseness. On examination there was evidence of marked loss in weight and strength. The liver was large and nodular. A caput medusae was present. The clinical impression was that of carcinoma of the stomach. Radiographic studies of the upper alimentary tract revealed a normal esophagus, stomach and duodenum. Roentgenograms of the colon and chest were normal. Esophagoscopy was not done. Tissue for biopsy was taken from the liver and found to contain carcinoma, mainly undifferentiated but with some squamous cell transition. Eighteen days after the radiographic studies of

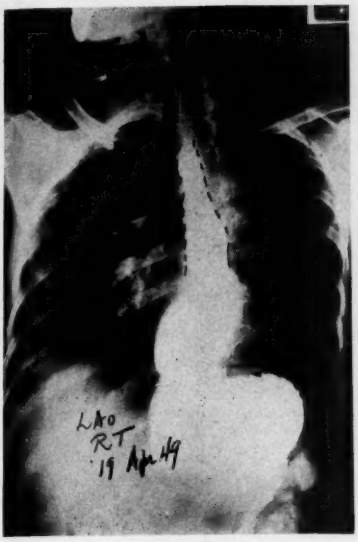


FIG. 3

FIG. 4

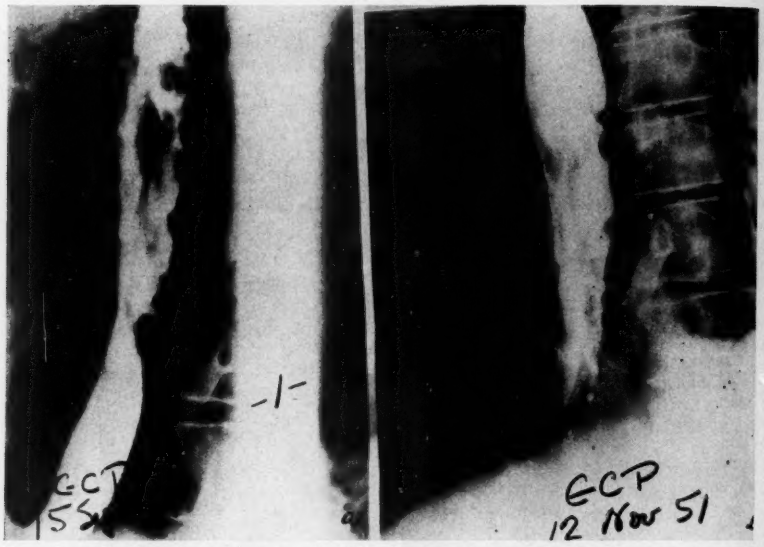
FIG. 3. Case 5. Photograph of a normal esophagogram, in April 1949. However, on esophagoscopy in February 1949, there was found a small carcinoma at the 22 cm. level (arrow pointing), proved by biopsy.

FIG. 4. Case 5. Photograph of the fresh specimen of excised esophagus. The esophagogastric junction is at the bottom. The nonobstructing carcinomatous ulcer, involving about 50 per cent of the circumference, is near the upper end.

the alimentary tract, he died. Autopsy revealed a tumor 3 by 1 cm. in diameter on the posterior wall of the middle third of the thoracic esophagus. Microscopic examination of this showed epidermoid carcinoma. There were metastases in the mediastinal and left gastric lymph nodes, and liver.

Comment: The above case illustrates another example of carcinoma of the esophagus not involving the major portion of its circumference and not detected on radiographic study, but yet easily discovered at autopsy. While establishment of the esophagus as the site of the primary tumor would have been only academic in this particular instance, it is reasonable to believe that this could have been done by esophagoscopy and biopsy.

Case 7. G. C. P., a white man, aged 67, was admitted to the hospital in September 1951, complaining of inertia and lassitude of six weeks duration. Since June 1951, he had had burning epigastric and substernal pain. The pain occurred after meals and after lying down at night. There was anorexia and a slight loss in weight. He had no dysphagia, nausea or vomiting. The physical examination was not remarkable. Roentgenograms of the esophagus showed a marked irregularity in the lower portion (fig. 5a). However, the irregularity smoothed when the esophagus was filled to a maximum. The radiographic impression was that of varices. On esophagoscopy, the mucosa was normal down to the 42 cm. level, at which level gastric mucosa was visible. No varices or other abnormality were found. It was recognized that varices, even if present, did not explain the symptoms. He was advised to return in several weeks. On readmission in November 1951, he stated that progressively increasing dysphagia began one week following his discharge from the hospital.



FIGS. 5a & 5b. Case 7. a. Photograph of the first esophagogram, showing a marked filling defect. Strange to say, at this time on esophagoscopy the mucosa was entirely normal down to the 42 cm. level. b. Photograph of the second esophagogram made six weeks later. At this time, esophagoscopy revealed an obstructing ulcerating carcinoma at the 36 cm. level, proved by biopsy.

The pain persisted and he had lost strength and 14 lbs. in weight. On examination he appeared chronically ill. There was a mass in the left upper quadrant of the abdomen. Roentgenograms of the esophagus showed a marked irregularity in the distal esophagus (fig. 5b), with slight stiffening of the walls. Again the radiographic impression was that of extensive varicosities. Esophagoscopy was repeated and an ulcerating obstructing lesion was found at the 36 cm. level. A biopsy revealed epidermoid carcinoma. Laparotomy was done and an extensive tumor was found in the left upper quadrant of the abdomen. The lesion was considered incurable, and he died in February 1952.

Comment: The above case represents an example of extensive carcinoma in the wall of the esophagus without recognizable alteration in the mucosa on the first esophagoscopy. In retrospect, the esophagoscopy should have been repeated during the first admission. However, in view of the normalcy on the initial examination, it is reasonable to believe the diagnosis could have been established at that time only by exploratory operation.

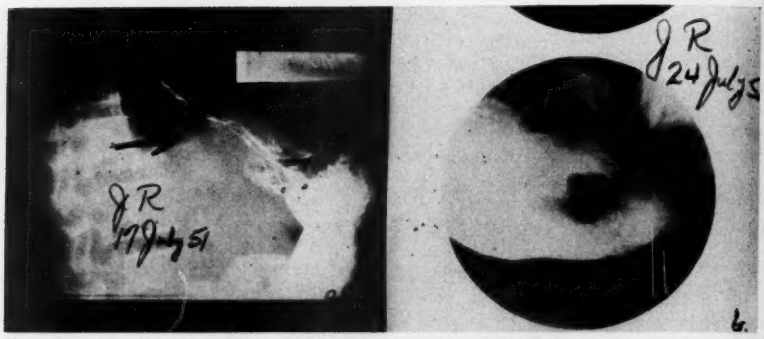
Case 8. M. M., a Negro woman, aged 64, was observed first in 1942 and found to have a non-toxic nodular goitre. In March 1950, she complained of dysphagia of five months duration and a mass in the neck. The goitre was still present. There was no evidence of hyperthyroidism. Roentgenograms revealed a mass in the neck displacing the trachea to the left. It was considered that the goitre was causing the dysphagia. Partial thyroidectomy was done. Microscopic examination showed a nodular goitre without evidence of malignancy. On her next visit to the clinic, it was noted that she was eating without any difficulty. However, she was readmitted in May 1950, because of dysphagia which was less severe than it had been initially. On examination, she was emaciated and dehydrated. Radiographic studies of the esophagus showed a constriction opposite the level of the tenth thoracic vertebra (fig. 6). Esophagoscopy revealed a tumor 38 cm. beyond the alveolar margin. A biopsy showed epidermoid carcinoma. The day following esophagoscopy she

died suddenly and unexpectedly. At autopsy, there was a carcinoma 4 cm. above the cardia with regional lymph node metastasis. No immediate cause of death was apparent.

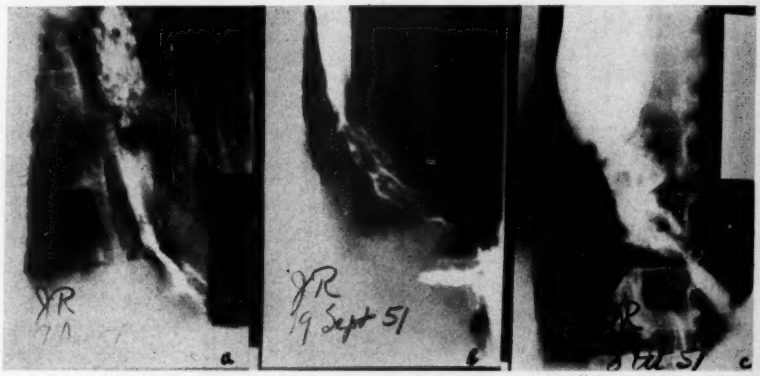
Case 9. J. R., a Negro man, aged 67, was seen in July 1951, with the complaints of constant pain in the epigastrium, and of food and even water choking him with a sensation of obstruction at the level of the sternal notch, of four months duration, with some loss in weight. Radiographic studies of the esophagus and stomach showed minor irregularities in the distal esophagus, without obstruction, considered to be due to early varices (fig. 7a), and a filling defect in the stomach considered to be due to a polyp (fig. 7b). He was admitted in August 1951, because of the polyp in the stomach. His chief complaints were the same as above with the addition of occasional vomiting with blood streaks in the vom-

FIG. 6. Case 8. Photograph of the esophagogram. There is a large filling defect corresponding to the 38 cm. level, due to carcinoma proved by biopsy.

itus. Physical and accessory examinations were not remarkable. Bronchoscopy was normal. On esophagoscopy, nothing abnormal was noted. The roentgenograms were repeated with the same findings (fig. 8a). Gastroscopy was done with visualization of the polyp in the stomach. Laparotomy was done. The gastric polyp was excised. A finger was not inserted into the lower end of the esophagus through the incision in the stomach. The liver was normal. Microscopic examination of the polyp revealed an adenoma, with no evidence of carcinoma. Recovery was uneventful. Afterwards he gained 13 lbs. in weight, but it was also noted that he limited himself to soft foods and milk. In September 1951, roentgenograms of the esophagus showed the same irregularity in the lower esophagus still considered most likely to be due to varices (fig. 8b). He was readmitted in October 1951, complaining of pain in the chest, abdomen and back. He had become too weak to walk, was unable to swallow without vomiting, and had lost weight. The physical examination was not remarkable except for weakness and dehydration. On esophagoscopy, the scope was passed to the cardia without any abnormality being noted. The roentgenograms were repeated and



FIGS. 7a & 7b. Case 9. a. Photograph of an esophagogram. There are minor irregularities in the distal esophagus. b. The rounded filling defect in the distal portion of the stomach is apparent.



FIGS. 8a, 8b, & 8c. Case 9. a. Photograph of an esophagogram with some raggedness in the distal esophagus. b. Photograph of an esophagogram with an abnormality in the distal esophagus. c. Photograph of the last esophagogram. There is a more marked filling defect in the distal esophagus. On the fourth esophagoscopy it was found to be due to carcinoma, proved by biopsy.

showed an irregular mucosal pattern in the distal 7 cm. of the esophagus with some stiffening of the walls (fig. 8c). The impression from examination of the radiograph for the first time was that of carcinoma being most likely. On another esophagoscopy, an obstructing mass was found 41 cm. from the alveolar margin. A biopsy did not reveal tumor. A fourth esophagoscopy was done, and it was noted that the lumen was rigid, narrowed and ulcerated between the levels of 40 and 45 cm. beyond the alveolar margin. A biopsy at this time revealed epidermoid carcinoma. The lesion was considered inoperable because of extreme malnutrition. In spite of roentgen ray therapy, he died in November 1951, eight months after the onset of the symptoms.

Comment: The last 2 cases cited represent examples of carcinoma of the esophagus overlooked initially because of the presence of other abnormalities upon which the symptoms referable to swallowing could be blamed, a cervical goitre in one case and a gastric polyp in the other. Also case 9 is comparable to case 7 in that the first two esophagoscopic

examinations were normal even though radiographic studies of the esophagus showed a persistent filling defect proved subsequently to be due to carcinoma. Also in case 9, the opportunity to discover the probable presence of carcinoma of the esophagus by exploratory operation was lost at the time of laparatomy by failure to insert a finger through the cardia via the gastrostomy for excision of the polyp. In view of the two normal esophagoscopies, it is believed that the diagnosis could have been established only by exploratory operation at that time.

DISCUSSION

The problem of obtaining better results in the treatment of carcinoma of the esophagus has several phases.[5] Certainly the most important phase to consider is that of early diagnosis. It is obvious that some method of determining the presence of a malignant tumor in the body prior to the onset of symptoms would be ideal, but such a method is yet to be found. In view of our present lack of knowledge concerning the cause of cancer, the duration of its presence prior to the onset of symptoms and the lack of availability of any method of treatment in most cases better than its complete surgical extirpation, it is equally clear that it is necessary to utilize to better advantage the diagnostic methods now available.

The diagnosis of a neoplasm in any organ or tissue not visible or palpable by the usual complete physical examination is most difficult to make early in its course. In the case of the esophagus, which is inaccessible to physical examination except for the short cervical segment infrequently involved by carcinoma, one has to rely upon an analysis of the history and accessory examinations in order to determine with reasonable accuracy the presence or absence of disease within it.

It follows that in any patient complaining of a sense of obstruction on swallowing, of unexplained digestive disturbances, hematemesis, melena, or loss in weight, or of any other symptoms possibly referable to the esophagus, such examinations are indicated. In such cases, a barium swallow is usually obtained first. In general, it is the custom of radiologists to omit making roentgenographic films of the esophagus if the fluoroscopic examination is normal. However, in known or suspected disease, films should be made also, as demonstrated in the foregoing case reports. If a filling defect is present on fluoroscopy or on the roentgenographic films, automatically esophagoscopy is indicated. It is not generally appreciated that even if the barium swallow is normal, esophagoscopy is indicated in addition. In our series, there were 6 patients having normal radiographic studies of the esophagus in the presence of histologically proved carcinoma. This has been of particular interest and significance, because our Department of Radiology has been staffed by unusually capable and cooperative colleagues. Therefore we must abandon the former concept that esophagoscopy is indicated only to determine by direct observation and biopsy the character of a lesion observed on radiographic examination. Henceforth, esophagoscopy must be considered an essential procedure in the diagnostic study of any patient in whom the presence of carcinoma of the esophagus is even remotely possible.

SUMMARY

Carcinoma of the esophagus is a highly malignant and rapidly fatal disease in the vast majority of cases, the three and five year survival rates being less than 1 per cent.

In order to obtain improved results in its surgical treatment, primary emphasis must be placed upon earlier diagnosis.

The reasons for delayed diagnosis, other than the usual lack of suspicion, are presented and analyzed.

Case histories illustrating mistakes and delays in diagnosis for the several reasons are cited.

It is pointed out that roentgenographic films of the esophagus should be made in addition to the fluoroscopic observations in patients with possible carcinoma of the esophagus, even if the fluoroscopic observations are normal.

It is stressed that in the study of patients with possible carcinoma of the esophagus, esophagoscopic examination on one or more occasions is necessary, even if the radiographic studies are normal.

REFERENCES

1. Adams, W. E., and Phemister, D. B.: Carcinoma of lower thoracic esophagus; report of successful resection and esophagogastrostomy, J. Thoracic Surg. *7:* 621 (Aug.) 1938.
2. Churchill, E. D., and Sweet, R. H.: Transthoracic resection of tumors of stomach and esophagus, Ann. Surg. *115:* 897 (June) 1942.
3. Gibbon, J. H., Jr.; Albritten, F. F., Jr., and Templeton, J. Y., III: Carcinoma of esophagus and gastric cardia, J.A.M.A. *145:* 1035 (April 7) 1951.
4. Pack, G. T.: The Problem of Malignant Melanoma. Lecture before the Second National Cancer Conference, March 4, 1952, Cincinnati, Ohio.
5. Parker, E. F.; Hanna, C. B., and Postlethwait, R. W.: Carcinoma of esophagus, Ann. Surg. *135:* 697 (May) 1952.
6. Sweet, R. H.: Results of radical surgical extirpation in treatment of carcinoma of esophagus and cardia, Surg., Gynec. & Obst. *94:* 46 (Jan.) 1952.

THE MANAGEMENT OF CHRONIC PANCREATITIS: A CRITICAL EVALUATION

GENE B. STARKLOFF, M.D.
WM. A. KNIGHT, JR., M.D.
ROBERT POLLOCK, M.D.

St. Louis, Mo.

Chronic relapsing or recurrent pancreatitis is the result of repeated attacks of acute pancreatitis, and the pathologic changes found in the pancreas are dependent upon the number and severity of the acute attacks. Different stages of the same pathologic process may result in edema, fibrosis, acinar and islet cell destruction, cyst formation, lithiasis and pancreatic calcification.

Various etiologic factors may cause chronic pancreatitis, and therapy must be based upon an appreciation of these, as well as upon the degree of pathologic alteration in the anatomy and physiology of the pancreas. Too frequently the assumption is made that one etiologic factor is responsible for the changes in chronic pancreatitis, when actually several modes of production of the disease are recognized. Opie[12] and Archibald[1] first suggested that chronic pancreatitis frequently was due to regurgitation of bile into the pancreatic duct. There is good evidence, both clinical and experimental, to show that when the pancreatic duct enters the common bile duct proximal to the ampulla of Vater, obstruction of the ampulla by edema, spasm, or stone may result in reflux of bile into the pancreatic duct. This common channel theory is tenable in about 60 or 70 per cent of patients. There remains approximately 30 to 40 per cent of patients with chronic pancreatitis in which infection, vascular damage, protein deficiency, trauma, or a combination of these are the causative agents.

Since there are multiple etiologic factors that may result in the same disease manifesting any stage of evolution, it, therefore, is perhaps improper to champion one method of therapy. There are advocates of sphincterotomy, gastrectomy, vagotomy and pancreatoduodenectomy. Methods of surgical treatment for chronic pancreatitis can be divided into four main categories: (1) *Procedures designed to prevent reflux of bile into the pancreatic duct.* In this group is included the elimination of common channel reflux by choledocholithotomy. Also included are procedures designed to interrupt the function of the ampulla of Vater. The methods of interruption are varied and include internal sphincterotomy, a method advocated by Mulholland[5, 6] and Doubilet, sphincteroplasty, which recently has been described by Jones and Smith,[8] and external sphincterotomy, which has been reported upon favorably by Gillette.[7] In the Gillette procedure an operation similar to a Ramstedt pyloromyotomy is done without opening the duodenum. By-passing procedures to prevent biliary reflux have been recom-

From the Department of Surgery, St. Louis University School of Medicine and The St. Louis City Hospital.

Presented during the annual assembly of The Southwestern Surgical Congress, September 21–23, 1953, Salt Lake City, Utah.

mended by Bowers and Greenfield.[2] These have been accomplished by choledochojejunostomy, utilizing the Roux Y principle. Transplantation of the duct of Wirsung has been done by Cattell[3] to prevent reflux. (2) *Procedures designed to eliminate the diseased pancreas.* Whipple[16] has reported 5 cases and Cattell[4] 15 cases of patients in whom total or partial pancreatectomy was done for the relief of advanced severe chronic pancreatitis. Clagett[15] and Zinninger[17] also have reported their experiences with this procedure. (3) *Procedures for the relief of pain.* Sympathectomy has been advocated by Mallet-Guy,[10] and later by Ray and Console.[13] They have used this operation for palliation in advanced cases of chronic pancreatitis. The rationale for this type of therapy is one of strict consideration of pain pathways which have been shown to traverse the splanchna. (4) *Miscellaneous procedures:* (a) Partial gastrectomy and vagotomy. This method of treatment, advocated by Richman and Colp,[14] has as its rationale elimination of the hormonal phase of gastric secretion, and thus reduction of hydrochloric acid production. The elimination of these two factors results in decreased secretin formation, and thus less pancreatic secretory activity. The authors believe that this causes less ductal distention and less pain. (b) Vagotomy. McCleery[9] and associates recently have reported the use of vagotomy in a small group of patients. They believe that vagotomy decreases pancreatic duct spasm; results in decreased enzyme secretion; and ameliorates the effect of the increased gastric acidity formed in response to excessive alcohol intake. (c) Biliary tract surgery. Many patients with chronic pancreatitis have associated cholecystitis and cholelithiasis with common duct stones. Possibly, biliary tract disease produces chronic pancreatitis on an infectious basis or leads to spasm of the pancreatic duct of the sphincter of Oddi. Many patients are improved by elimination of biliary tract diseases with no other therapy.

ANALYSIS OF PATIENTS STUDIED

In the years 1942 to 1952, 119 patients with chronic pancreatitis were admitted to the St. Louis City Hospital. Our experience with the management of these patients forms the basis of this report. In many of the earlier patients (1942 to 1946), the method of management would have been changed in light of our present knowledge, but we have gained valuable information by study of these earlier patients. It is not the purpose of this report to offer a detailed summary of all cases, but rather to record our impressions of the group in general.

Age: Chronic pancreatitis is more frequently encountered in the aged than is generally realized. Obviously, the age at which the diagnosis is made is not the age of onset since many patients have had symptoms for months or years. It is interesting to note, however, that 23.5 per cent of our patients were over 65 years of age.

Sex: There is, roughly, an equal sex distribution, which is noteworthy only relative to the fact that gallbladder disease is approximately four times as frequent in females. With the large association in this study between gallbladder disease and chronic pancreatitis, we believe that if the gallbladder disease had been the etiologic agent resulting in chronic pancreatitis, a higher incidence in

the female might have been expected. Forty-seven and two tenths per cent of the patients in this series were males.

Diagnosis: Diagnosis can not be arrived at by symptoms alone. This is particularly true of the early case with minimal or moderate alteration in pancreatic structure and activity. In patients with severe chronic pancreatitis the diagnosis can be suspected by the presence of steatorrhea, diabetes mellitus, weight loss and severe, constant, girdle-like upper abdominal pain. One of us (W. A. K., Jr.)[11] previously has reported on the symptoms of 58 cases of chronic pancreatitis. An analysis of the present group of cases shows no essential deviation from that report. The keystone of diagnosis is a high index of suspicion. Realization that chronic pancreatitis may be responsible for almost any gastrointestinal symptom is of paramount importance. Once suspicion is aroused, it may be verified in a high percentage of patients by employment of random diastase determinations. The serum diastase is universally recognized as elevated during acute exacerbations of chronic recurrent pancreatitis. It is generally thought that diastase values quickly fall to normal levels, even though the pancreatitis continues. Our experience leads us to doubt the validity of this concept.

Diastase determinations are done by the method of Somogyi. Normal individuals have a fairly constant serum diastase from day to day. We believe that the normal range for serum diastase should be considered as 80 to 150 units. Values from 150 to 200 are high normals, and readings above 200 are definitely abnormal. Levels below 80 units are indicative of severe pancreatic insufficiency, if liver damage can be ruled out.

Diastase values in normal individuals and in individuals with disease, exclusive of pancreatic disease, are seldom elevated. We have found that 64.4 per cent of patients with chronic pancreatitis have serum diastase levels above normal even when in remission. Many of the patients in this present series have had serum diastase values above 300 units when asymptomatic and when clinically they are in a period of remission. Diastase determinations must be repeated at intervals, regardless of symptoms, if pancreatitis is suspected. In our hands, random diastase values have been rewarding as an aid in the establishment of a diagnosis.

In the 119 cases herein reported the diagnosis was made by a combination of history, physical and roentgenographic findings, as well as abnormal diastase values. In order to merit inclusion in this group, patients must have had one or more attacks; a duration of complaints of six months or more; and abnormal diastase values on one or more occasions. Ninety per cent of the patients in this group had elevated diastase values. The remaining 10 per cent had abnormally low values. In the group with low values, at least two of the following findings were present: diabetes mellitus, steatorrhea, weight loss, severe upper abdominal pain, roentgenographic evidence of calcification of the pancreas, or pancreatic stones.

Therapy: After the diagnosis of chronic pancreatitis has been established, attention should be turned to investigation of the biliary tract. This is the first echelon of attack, and there will be found a substantial group of patients who will have preoperative demonstrable pathologic changes in the gallbladder or

common bile duct. Thirty-one and nine-tenths per cent of the patients in this group were found to fall into this category. It should be emphasized that acute pancreatitis may produce abnormal cholecystogram. We repeatedly have had the experience of having a nonfunctioning gallbladder reported by the radiology department during an acute exacerbation of pancreatitis, and normal function found after subsidence of the acute attack. Cholecystectomy and exploration of the common duct with choledocholithotomy when indicated, can be expected to produce good results in these patients. Pancreatic pathologic changes found at operation, in our experience, has been minimal or moderate. Seventy-six and six-tenths per cent of patients so treated have had good results. Many of this group have been followed over six years. The majority of poor results in this group could be attributed to failure to explore the common bile duct—a grave omission when operating upon the biliary tree in patients with chronic pancreatitis.

Frequently patients are admitted because of an acute exacerbation of chronic pancreatitis. Conservative therapy is indicated in this group. Our plan of management includes continuous gastric suction and the parenteral administration of large doses of atropine or atropine-like drugs. This is done in order to minimize the secretory activity of that pancreas. Penicillin is administered, since there is evidence that pancreatitis may have an infectious basis. Fluid and electrolyte imbalances are corrected. Blood volume deficits are restored. Demerol is used to allay pain. Morphine is avoided because of its spastic effect on the sphincter of Oddi. When indicated—because of pain—thoracic splanchnic block is used.

When the acute attack has subsided a thorough evaluation of the patient is begun. Special attention is given to cholecystography, radiographic investigation of the gastrointestinal tract, and evaluation of liver function. In patients with chronic pancreatitis, with no demonstrable associated pathologic changes, a period of intensive medical therapy is warranted. Since alcohol is recognized as a possible precipitating factor in pancreatitis, strict abstinence from alcohol is advised. Frequent bland high protein feedings are given because the relation between available protein and lipotrophic agents in the production of experimental pancreatitis has raised a question as to whether protein depletion in human beings, either primary or secondary, may initiate pancreatitis. Based upon this concept, large doses of lipotrophic substances, such as methenamine and choline, are administered. We have supplemented these agents with Vitamin B-12 parenterally, and the results with this therapy to date suggest that patients have a much better appetite; gain weight; have fewer subjective symptoms and less chance for recurrent attacks. Atropine, Banthine and allied drugs are used to decrease both sphincter spasm and pancreatic activity. If diabetes is present it should be controlled, and in patients with evidence of pancreatic enzyme deficiency, pancreatin and tween 80 are administered. It has been our experience that such a trial period of medical management is justified and that a definite group of patients will respond to such a regime. Thus, it does not seem warranted to subject all patients with chronic pancreatitis to exploration.

Failure to respond to medical management, or recurrent attacks, constitutes

definite indication for surgical intervention, which should be done early before the pancreas has been subjected to multiple repeated attacks resulting in marked alteration in its normal architecture and function. The best interests of the patient are served if the operative findings at exploration dictate the type of surgical procedure employed. The extent of pathologic changes in the pancreas is most important in arriving at a decision as to proper surgical therapy. We have grouped these changes into three main categories: *Minimal*, *Moderate*, and *Severe*. *Minimal* alterations consist of slight nodularity and edema. It is frequently difficult at exploration to be sure by any method short of biopsy that the pancreas has been involved in previous attacks. *Moderate* pathologic change consists of rather marked nodularity, definite edema, evidence of old fat necrosis, and occasionally minimal calcification. In the category of *severe* pathologic changes is included marked fibrosis with nodules that are firm, large and frequently difficult to differentiate from neoplasm, marked edema, frequently calcification and interductal stones. Pseudocysts may be present. Adhesions are dense and there is evidence in the adjacent fat that there have been repeated severe attacks. We frequently have found that the pancreatic duct is soft and easily demarcated from the surrounding pancreatic parenchyma. On one occasion 200 cc. of pancreatic juice was aspirated from a dilated duct. Cattell has stressed that the findings of a dilated pancreatic duct frequently is pathognomonic of malignant obstruction proximal to the dilatation. We have not been able to confirm this finding, and in advanced chronic pancreatitis we believe that such ductal dilatations are not unusual.

In patients with minimal and moderate pathologic changes in the pancreas, multiple methods of surgical treatment have been used. The choice of therapy largely will be dictated by choledochostomy, operative cholangiography and demonstration of sphincter spasm. If a spastic or hypertrophic sphincter is demonstrated, either by cholangiography or by transduodenal exploration of the sphincter of Oddi, sphincterotomy is indicated. We do not recommend endocholedochosphincterotomy because we believe the transduodenal visualization of the sphincter is preferable. By this means injury to the pancreaticoduodenal artery is minimized. Exploration of the sphincter of Oddi via the duodenal route makes possible a wedge excision of the muscular fibers of the sphincter—a plan that is preferable to simple section which may result in fibrosis and a reconstitution of the original mechanism of spasm. We have had the experience of apparent healing of the sphincter and return of spasm. Similar cases have been reported and have led to ingenious methods of sphincterotomy in an attempt to overcome this possibility. We have done five sphincterotomies by the transduodenal route, four of them with excellent results. All of these were done in patients who had minimal or moderate pancreatic pathologic changes and demonstrable sphincter spasm. The one poor result apparently was on the basis of rehealing of the sphincter of Oddi cut by simple section. These cases are not a true reflection of the number of indications we have had for sphincterotomy, for it is only in the past three years that we have had adequate technical facilities for operative cholangiography. Five patients in our series have had biliary intestinal

anastomosis. These have consisted of anastomosis of the common bile duct to the jejunum by the Roux Y technic as advocated by Bowers and Greenfield, or cholecystojejunostomy utilizing the Roux Y principle. Two patients had good results, while 3 have had unsatisfactory results with recurrence. The technical problems involved in this short-circuiting procedure and the possibility of stricture at the anastomatic site must be seriously considered. We believe that biliary intestinal anastomosis has little to recommend it over adequate wedge excision of the sphincter of Oddi since both have as their rationale prevention of reflux.

Gastrectomy and vagotomy each have been used only once in our series. The results in both patients have been classed as good. We believe that this procedure has been used in too few cases for adequate evaluation, and it impresses us that it is a devious approach to the therapy of chronic pancreatitis. It is certainly not justified in advanced pancreatic pathology and we do not recommend it on the basis of the results published to date. Sympathectomy was not used in any of the cases herein reported. Our goal has been prevention of progression of the disease or its extirpation, and not palliation, which, if accomplished, often is of a transitory nature. Nineteen patients, or 15.9 per cent, with chronic pancreatitis had maximal pancreatic pathologic changes. All of these patients had associated findings and symptoms indicative of insufficiency of pancreatic hormones and enzymes. Pain was a prominent symptom in all. A large percentage were morphine addicts, frequently of iatrogenic origin. Gastrointestinal symptoms were severe and cachexia was marked. It is in this group of patients that partial pancreatectomy merits careful consideration. Although pancreatectomy is a formidable procedure, when the disease has advanced to the stage of pancreatic insufficiency and the pathologic and physiologic alterations in the gland are marked, extirpation of the diseased organ seems the only rational procedure in a desperate situation. We have been impressed that many of these patients are in as serious a condition as if they were suffering from pancreatic neoplasm and heroic measures are applicable, and, in our hands, have been satisfactory. Five brief case reports of patients with chronic pancreatitis treated by partial pancreatectomy follow.

CASE REPORTS

Case I. H. A., a 40 year old white woman, had a long history of alcoholic excess and undiagnosed upper abdominal pain beginning in 1948. A diagnosis of chronic recurrent pancreatitis was made elsewhere in 1949, on the basis of symptoms and elevated diastase values. Medical treatment was carried out until 1952. The patient at this time had weight loss, voluminous fatty stools, constant upper abdominal pain, and was a narcotic addict. Cholecystectomy, common duct drainage and sphincterotomy were done in 1952 in another city. T tube drainage of the common duct was instituted and continued for three months. In January 1953 she was reexplored because of persistent pain, but no definite procedure was done. She was seen by us in January 1953. Diastase values at this time were 30 units, 29 and 27 on a random sampling. Operation was done in February 1953. At this time the patient weighed 72 pounds. The findings at operation included massive edema, fibrous adhesions, multiple nodules throughout the head and body of the pancreas, and a dilated pancreatic duct containing calculi. Aspiration of the pancreatic duct revealed 200 cc. of pancreatic juice. Pancreaticoduodenectomy was done with resection of all but 5 cm. of the distal pancreas. The distal stump of the pancreas was closed and gastrointestinal

continuity established. The postoperative course was complicated by a right upper quadrant abscess which was drained in March 1953. The subsequent course has shown no evidence of diabetes; digestion has been normal without steatorrhea; weight gain has occurred, and the patient is free from pain. She is no longer dependent on narcotics and classifies her result as excellent. Diastase values have risen to normal levels.

Comment: This patient with history, physical, roentgenographic and laboratory findings typical of advanced chronic pancreatitis and pancreatic insufficiency has responded well to pancreatectomy. In view of the findings at exploration, no procedure short of radical extirpation of the diseased pancreas could have been expected to relieve the patient's symptoms. The multiple previous operative procedures made the technical performance of pancreatectomy rather difficult. Despite failure to re-establish continuity between the distal pancreas and the gastrointestinal tract, normal digestion and weight gain have resulted.

Case II. J. W., a 33 year old white man, was admitted to the St. Louis City Hospital in February 1953 with a history of abdominal pain of 4 years' duration. He had lost 40 pounds in weight, had steatorrhea, and mild diabetes. He was an alcoholic and a narcotic addict. Random diastase values were 50, 60 and 75. A roentgenogram of the abdomen showed calcification of the pancreas. This patient was treated by the medical service until March 1953. Then a pancreaticoduodenectomy was done with resection of the proximal ¾ of the pancreas. The distal stump of the pancreas was closed. The pancreas showed marked fibrosis, edema and calcification, and a cyst was present in the mid portion of the body. The postoperative course was complicated by a severe electrolyte imbalance which was corrected with difficulty. The patient was discharged in June 1953, gaining weight, free of pain, and no longer dependent upon narcotics. Diabetes is present, but is mild. Digestive disturbances are minimal, although some steatorrhea is present. This is controlled by pancreatin.

Comment: The advanced pancreatic pathologic change in this patient could, in our opinion, be treated only by pancreatectomy. Exclusion of the distal pancreas from the gastrointestinal tract has not augmented pancreatic insufficiency and diastase values are up from the preoperative levels.

Case III. L. S., a 38 year old white woman, was admitted to the St. Louis City Hospital in October 1950 for the fourth time, because of diabetes mellitus, weight loss, chronic recurrent gastrointestinal symptoms, peripheral neuritis and advanced pulmonary tuberculosis. Diastase value in 1948 was 130 units and in 1949 was 50 units. Previous treatment had included antibiotic therapy, insulin, pancreatin, tween 80, and supplemental vitamins. Findings at this admission were severe diabetes with diabetic acidosis and diabetic retinopathy, and severe pancreatic insufficiency, as evidenced by steatorrhea, abdominal pain and weight loss. Diastase values varied from 31 to 48 on random sampling. A regime directed at the control of the diabetes and gastrointestinal symptoms was instituted. Because the symptoms were thought to be due to recurring attacks of pancreatitis, exploration of the pancreas was advised. At operation there was marked fibrosis and calcification of the tail of the pancreas. Calculi and ductal distention were present. Since the major portion of the disease was confined to the tail of the pancreas, distal pancreatectomy was done with resection of the tail and body of the gland. The postoperative course was smooth. Readmission to the hospital for study in July 1951 revealed weight gain, normal stools, and a reduction in the severity of the diabetes. The serum diastase values, which for several years prior to operation were consistently lower than 50 units, measured 70 to 160 units. This patient remained well and free of symptoms until she died as the result of a cerebral vascular accident in October 1952.

Comment: The improvement in this patient's diabetes after partial pancreatectomy is interesting and probably can be explained on the basis of general improvement in her condition and in her ability to assimilate her diet, resulting from the improvement of her pancreatic insufficiency.

Case IV. R. S., a 33 year old white woman, with a long history of chronic digestive

disturbances and upper abdominal pain, was first admitted to the St. Louis City Hospital in 1941. A diagnosis of pancreatitis was made on the basis of elevated diastase values at this time. Gallbladder roentgenogram examinations were normal, and the patient was treated by a medical regime. In February 1948 she was readmitted because of upper abdominal pain. A mass in the left upper quadrant of the abdomen was discovered on examination. Roentgenologic studies revealed the stomach to be pushed forward and the left half of the transverse colon downward. A diagnosis of pancreatic cyst was made. Exploration was done in March 1948 and severe pancreatic fibrosis and edema were found. The cyst, which occupied the tail of the pancreas, was marsupialized to the anterior abdominal wall. Symptoms of severe pancreatic insufficiency developed and the patient complained of constant upper abdominal pain. She was a narcotic addict. She was discharged from the hospital to be readmitted in October 1948. Diastase values at this time were 45 and 50 units. On Oct. 26, 1948, the patient was reoperated upon and a distal pancreatectomy was done. The postoperative course was uncomplicated and she has remained well. Diastase values on Nov. 13, 1948 were 126 units. The patient describes her result as good.

Comment: Distal pancreatectomy, when applicable, is a much less formidable procedure than proximal pancreatectomy. This patient had disease confined mainly to the body and tail of the gland and the removal of the diseased distal pancreas seems to have resulted in improvement of pancreatic function.

Case V. This patient was a 40 year old white woman who had had repeated admissions to the St. Louis City Hospital, on both the medical and psychiatric divisions, with diagnoses of acute alcoholism, psychoneurosis, drug addiction and Laennec's cirrhosis. She was admitted June 1952 with chronic gastrointestinal disturbances, abdominal pain and a left upper quadrant mass. A diagnosis of pseudocyst of the pancreas was made because of elevated diastase values and a roentgenographic deformity on gastrointestinal examination consistent with a pancreatic cyst. In July 1951 she was explored and calcification, fibrosis, edema and cyst formation was found in the pancreas. The pseudocyst was marsupialized to the abdominal wall. After a stormy postoperative course, the patient was discharged, only to be readmitted 5 times in the ensuing 30 months because of pain, barbiturate intoxication, alcoholism, and drug addiction. Random diastase values during these admissions were all below 50 units. On Nov. 20, 1952 she was reoperated upon and a partial pancreatectomy was done. The tail and the body of the pancreas showed replacement with fibrosis, edema, and cyst formation. The postoperative course was smooth. The patient was discharged, gaining weight and with normal diastase values. She returned to the hospital in September 1953 complaining of abdominal pain. She is well nourished and it is the opinion of the Psychiatric Department that continued drug addiction and alcoholism are her essential problems.

Comment: This patient emphasizes the difficulty in evaluation of patients with advanced pancreatic pathologic changes, since so many of them are narcotic and alcoholic addicts. If her pain is real, thoracolumbar sympathectomy will be considered as a palliative measure. Her weight gain and improvement in digestion indicate that the decision to do distal pancreatectomy was valid.

DISCUSSION

We have been impressed by the general failure to obtain even fairly good results on patients with chronic pancreatitis with advanced pathologic changes in the pancreas. In these patients with severe alteration of the normal architecture of the gland, pancreatic insufficiency has been a constant accompanying factor. This has led us to recommend partial pancreatectomy in these advanced cases, and in our hands this has been rewarding. There has been minimal mor-

bidity and no mortality in the 5 patients whose cases are herein reported, and the results have been good in 4, and fair in 1. In reviewing our patients with advanced pancreatic disease, we wonder if certain patients with advanced pathologic changes, who have had less radical measures, would not have been benefited more by the aggressive procedure of extirpation of the diseased gland. Because of the socio-economic status of our patients long term follow-up studies are difficult, but we anticipate that many of our patients with advanced pancreatitis, who have had less radical procedures, will eventually return demanding relief from persistent disease.

Partial pancreatectomy, after less radical procedures have been tried without avail, is a much more formidable procedure than when done as a primary operation. The technical difficulties are often compounded by the presence of severe nutritional problems, drug addiction of long standing, or diabetes. After partial removal of such a *burned-out* pancreas we have been impressed with the return to normal of diastase values, decrease in steatorrhea, and the ease of control of diabetes. We wish to stress that *total* pancreatectomy does not seem warranted as a primary procedure and that *partial* pancreatectomy is advised only in certain patients with severe pancreatic pathology and evidence of pancreatic insufficiency.

SUMMARY

Our experience in the management of 119 cases of chronic pancreatitis is presented.

The value of random diastase determinations as an aid in the diagnosis of relapsing pancreatitis is emphasized.

The necessity of correlating the etiologic agent in pancreatitis with the type of therapy chosen is stressed.

Partial pancreatectomy offers the best chance for relief in certain patients with advanced chronic pancreatitis and pancreatic insufficiency.

REFERENCES

1. Archibald, E.: Experimental production of pancreatitis in animals as result of resistance of common duct sphincter, Surg., Gynec. & Obst. *28:* 529 (June) 1919.
2. Bowers, R. F., and Greenfield, J.: Choledochojejunostomy, its role in treatment of pancreatitis, Ann. Surg. *134:* 99 (July) 1951.
3. Cattell, R. B.: Anastomosis of duct of Wirsung; its use in palliative operations for cancer of head of pancreas, S. Clin. North America *27:* 636 (June) 1947.
4. Cattell, R. B., and Warren, K. W.: Choice of therapeutic measures in management of chronic relapsing pancreatitis and pancreatolithiasis, Gastroenterology *20:* 1 (Jan.) 1952.
5. Doubilet, H., and Mulholland, J. H.: Surgical treatment of recurrent acute pancreatitis by endocholedochal sphincterotomy, Surg., Gynec. & Obst. *86:* 295 (March) 1948.
6. Doubilet, H., and Mulholland, J. H.: Surgical treatment of pancreatitis, S. Clin. North America *29:* 339 (April) 1949.
7. Gillette, L.: External sphincterotomy for pancreatitis, Ann. Surg. *138:* 24 (July) 1953.
8. Jones, S. A., and Smith, L. L.: Transduodenal sphincteroplastomy for recurrent pancreatitis, preliminary report, Ann. Surg. *136:* 937 (Dec.) 1952.
9. McCleery, R. S.; Kesterson, J. E., and Schaffarzick, W. R.: Clinical study of effect of vagotomy on recurrent acute pancreatitis, Surgery *30:* 130 (July) 1951.
10. Mallet-Guy, P., and de Beaujeu, M. J.: Treatment of chronic pancreatitis by unilateral splanchnicectomy, Arch. Surg. *60:* 233 (Feb.) 1950.

11. Muether, R. O., and Knight, W. A., Jr.: Chronic recurrent pancreatitis. I. Clinical and laboratory aspects, Gastroenterology *12:* 24 (Jan.) 1949.
12. Opie, E. L.: Etiology of acute hemorrhagic pancreatitis, Bull. Johns Hopkins Hosp. *12:* 182, 1901.
13. Ray, B. S., and Console, A. D.: Relief of pain in chronic (calcareous) pancreatitis by sympathectomy, Surg., Gynec. & Obst. *89:* 1 (July) 1949.
14. Richman, A., and Colp, R.: Chronic relapsing pancreatitis treatment by subtotal gastrectomy and vagotomy, Ann. Surg. *131:* 145 (Feb.) 1950.
15. Waugh, J. M., and others: Total pancreatectomy: symposium presenting four successful cases and report on metabolic observations, Proc. Staff Meet., Mayo Clin. *21:* 25 (Jan. 23) 1946.
16. Whipple, A. O.: Radical surgery for certain cases of pancreatic fibrosis associated with calcareous deposits, Ann. Surg. *124:* 991 (Dec.) 1946.
17. Zinninger, quoted by Whipple, A. O.[16]

MEDULLARY NAILING OF FRACTURES

DENMAN C. HUCHERSON, M.D.

Houston, Texas

For the past few years medullary nailing of fractures has been widely and perhaps over-enthusiastically practiced in this country. Articles have appeared in the literature advocating medullary nailing of every long bone of the body. Recently I saw a patient in whom a medullary pin was placed in a fracture of the shaft of the fibula. With this line of reasoning I cannot concur. The femur is the most suitable bone in the body for this procedure, both anatomically and economically. I can see no reason for subjecting a patient to an open operation with either plating or intramedullary fixation when a simpler, known and tried method will suffice. Intramedullary fixation of fractures of both bones of the forearm has proved unsatisfactory in our experience. Similarly, such treatment of fractures of the tibia seems to me to be anatomically inadequate. I believe that in an occasional fracture of the humerus, medullary fixation may become necessary. Fractures of the clavicle can most easily be handled by this method.

FEMUR

Medullary nailing of the femur is the most important innovation in the treatment of fractures in recent years. For a patient to be ambulatory within a week or 10 days after such a serious injury is amazing. The technic of medullary nailing of the femur is well understood by this group. In 1950, I published in detail the technic practiced by our group, which was briefly as follows:[2]

At operation the patient is placed on his unaffected side with the involved extremity flexed to 90 degrees at the hip and knee. A posterolateral incision is made, exposing the fracture site. The proximal end of the fracture is delivered into the incision and the rod is manually inserted upward. If resistance is met, a smaller rod is used. Previously we had used reamers in the form of large drill bits, but now we believe that the manual method of insertion is better. If the rod can be inserted manually as far as the trochanteric region with moderate resistance it is believed that the size of the rod is satisfactory. Attempts to measure the diameter of the medullary canal radiographically have not proved satisfactory. After the nail has been driven past the fracture site the fracture is reduced and the nail driven into the distal fragment. Roentgenograms always should be made on the operating table to determine the situation of the nail before closing the incision.

A few years ago in reporting 74 cases of fracture of the femur treated by medullary fixation, I made the statement that complications had been surprisingly few, and that in this series, in which the diamond-shaped nail had been used, we considered the results to have been excellent. In preparing this paper

From the Department of Orthopedic Surgery Baylor University College of Medicine, Houston, Texas. Read before the Panel on Trauma, American College of Surgeons, New York, Sept. 23, 1952.

I have recently reviewed 200 cases of fracture of the femur treated by this method and I can no longer make the statement that complications are few. In this series many of these cases had been treated elsewhere and had been referred for consultation or treatment. I would like to present some of the complications that unfortunately are occurring. Most of these complications are due to faulty technic. Migration of the rods is a problem that frequently arises. I have never seen a rod migrate distally, although I have been told by some that this occurs. I do not see how a rod could migrate distally unless it had originally been driven into the knee joint. Very frequently, however, the rod does migrate cephalad. This particularly is true when the fracture is a high one. This is not considered to be a serious complication, as a rod very easily can be redriven under local anesthesia. Separation of the fragments is another complication that is seen frequently, which will delay healing and callus formation. In driving the rod the fragments may be distracted and healing delayed. This very readily can be overcome by impacting the fragments by forceful pressure against the knee.

Complications arising from gross carelessness of technic are often seen. These errors include driving the nail into the knee joint; failure properly to reduce the fracture; and missing the distal fragment, although the fracture was under direct observation; using too small a nail, which allows rotation of the distal fragment; and using too large a nail, which very frequently will split the shaft of the bone, and on one occasion was known to fracture the neck of the femur due to excessive pounding. Painful bursa formation over the protruding nail is almost routine when it is allowed to protrude too far. Impossibility of withdrawing the nail has been encountered on two occasions. There has been one serious and one fatal case of osteomyelitis which developed following medullary fixation in this series. There has been 1 proved case of fat embolisn. The patient recovered.

So we see this procedure is not a foolproof one, and is one not to be undertaken by those whose surgical skill and judgment are inadequate.

HUMERUS

It was a well known fact, and still is well known to many, that more than 90 per cent of the fractures of the humerus can be adequately and satisfactorily treated by the hanging cast. It was my privilege to help popularize this method of treatment. In 1941 we reported 305 consecutive cases of fractures of the shaft of the humerus treated by the hanging cast with excellent results.[1] Fractures of the shaft of the humerus so treated unite in six to eight weeks and I can see no reason for doing open reduction upon this type of fracture in the uncomplicated case. If open reduction of the humerus is indicated, in such cases as radial palsy, bilateral fractures of the humerus, and other mitigating circumstances, I certainly advocate intramedullary fixation and have used it on a few occasions. I believe that the Rush nail is the most adequate implement in fixing these fractures.

CLAVICLE

Our staff for some time has been very enthusiastic about internal fixation for fractures of the clavicle. With closed methods of treatment of these fractures

the cosmetic and anatomic results are almost universally bad. There have been over 200 methods described for treating such fractures. All of them are painful, uncomfortable and inadequate. Internal fixation of the clavicle is a relatively simple procedure. A small incision is made over the fracture site; the pin is drilled out to the lateral fragment; the fracture reduced and the pin is drilled back across the fracture site, approximately 2 inches across the fracture line; the pin is cut beneath the skin. Closing the skin with a subcuticular stitch affords a very excellent cosmetic result. This method permits the patient to return to work at an early date and frees him from the cumbersome apparatus so frequently applied in treatment of this fracture.

Moore[3] has reported 25 cases of fracture of the clavicle treated by internal pin fixation. He believes that the experienced surgeon can do this procedure in 30 minutes. He stated that the majority of these patients left the hospital on or before the third postoperative day and many left the first postoperative day. All of the patients had 80 per cent full range of motion of the shoulder, without pain, within 24 hours following operation. Many of his cases were men engaged in occupations requiring strenuous physical activity, and these as a rule were able to return to their occupations within five days following operation. All of the fresh fractures united within an average of 10 weeks with excellent functional and cosmetic results.

CONCLUSIONS

It is my opinion that medullary fixation of fractures is indicated only in fractures of the femur, occasionally the humerus, and almost routinely in the clavicle.

Medullary fixation of fractures of both bones of the forearm, in our hands, has been most unsatisfactory. Delayed or nonunion has been the rule rather than the exception. I have completely abandoned this method in the treatment of fractures of the bones of the forearm.

A believe that fractures of the tibia are better treated by the Eggers contact splint, as it appears that the tibia is not anatomically suited to medullary fixation. Enough stability of the tibial fragments cannot be obtained to eliminate additional plaster fixation. Boehler has noted that anatomic reductions in fractures of the tibia often cannot be maintained by this method.

REFERENCES

1. Griswold, R. A.; Hucherson, D. C., and Strode, E. C.: Fractures of humerus treated by hanging cast, South. M. J. *34:* 777 (July) 1941.
2. Hucherson, D. C.: Medullary fixation of femoral shaft fractures, Am. J. Surg. *80:* 666 (Nov.) 1950.
3. Moore, T. O.: Internal pin fixation for fracture of clavicle, Am. Surgeon *17:* 580 (July) 1951.

EDITORIALS

INGUINAL HERNIA IN THE OLDER AGE GROUP

Inguinal hernia is the most common congenital anomaly, and its successful surgical correction in the young offers little difficulty. However, the problem may be more complicated in the older age groups. Any patient in middle life or older who presents himself complaining of an inguinal hernia, especially of the direct type, deserves careful over-all evaluation before repair is recommended. While a low recurrence rate for this group may be recorded by those especially interested in the problem, it is doubtful if the results are universally so favorable. A thorough knowledge of the anatomy of the inguinal region as well as familiarity with a variety of meticulous methods of repair is a prerequisite for insurance of a low recurrence rate.

Since the diagnosis of inguinal hernia rarely is a problem and correction by surgery is universally accepted, there is a tendency to proceed without sufficient evaluation of the patient, especially in the older age groups.

Why should a man develop an inguinal hernia of any type late in life? If he has had a hernia for years why has he finally reached a decision to have it repaired? All too frequently the obvious diagnosis of hernia is readily accepted by patient and physician as an indication for surgery without due consideration of other possible reasons which may be responsible for the individual seeking medical attention. Disease within the chest associated with a productive cough or hidden pathology within the gastrointestinal tract may be responsible for symptoms which the patient falsely believes can be erased by a repair of the obvious hernia. Of greater importance, especially in the presence of direct hernia, is obstructive disease of the genitourinary system. Such mistakes are so common as to be a favorite topic of discussion among urologic surgeons.

It would seem to be a worthwhile policy to insist that the majority of patients above the age of 50 years have an adequate evaluation of the prostate gland before repair of an inguinal hernia. Furthermore, if there is any suggestion of complaints referable to the gastrointestinal tract, complete upper and lower gastrointestinal roentgenologic studies should be made. Films of the chest are accepted as a routine affair.

Last but not least is the problem of obesity. Other than the general benefits to be derived from losing weight, the patient should be acquainted with the fact that there is no better way to decrease the chance of recurrence. Like all other things in medicine and surgery, individualization and common sense are important in the management of the *lowly* inguinal hernia. Herniorrhaphy may not be the most glamorous operation in surgery today, but it is one of the most common and as such, is entitled to the very best efforts from all concerned.

ROBERT M. ZOLLINGER, M.D.

Ohio State University
Columbus, Ohio

THE SURGICAL TREATMENT OF DIRECT AND FEMORAL HERNIA

Since the 1890's when Halsted, Bassini and Ferguson described their individual methods for the surgical repair of inguinal hernia, the literature has been replete with major and minor variations on these technics. Each of the multitude of authors on this subject has presented a method which, in his opinion, would reduce the likelihood of recurrence of this disease. Only a few have been brash enough to publish the statement that in their hands the problem has been solved. As Dr. A. R. Koontz of Baltimore has so aptly said, "It is somewhat disconcerting, indeed almost humiliating, for a competent surgeon not to be able to assure a patient that he can be definitely cured surgically of such a supposedly simple condition as a small inguinal hernia. Yet a glance at the recurrence rates is enough to assure even the most naive surgeon with the utmost self confidence that he cannot promise his patient that he will certainly cure him. This is enough to give pause not only to the patient but to the surgeon as well."

Although we are far from general agreement on the subject of groin hernias, it is certainly the consensus of opinion in the current literature that the recurrence rate is higher in the large direct hernias than in the small indirect or femoral variety. Wangensteen in 1949 reported a recurrence rate of 30 per cent in direct hernias repaired at the University of Minnesota Hospital, and as McVay stated at that time he knew of 67 recorded operations for the repair of inguinal and femoral hernias so the problem is certainly not solved. I would like to make it clear that I have no panacea for the repair of inguinal hernia. However, as a crusader for the McVay technic, it is my firm conviction that the proper use of the transversus layers and Cooper's ligament in the repair of direct and femoral hernias has been responsible for an important reduction in the incidence of recurrence.

The method described by McVay and Anson in 1942 has been at least gingerly applied at most of the medical centers throughout the country, and although it falls far short of general acceptance, it has certainly been more widely used than any other single method since that described by Halsted. There is at least one startling fundamental difference between his procedure and the time honored method of sewing the conjoined tendon to Poupart's ligament, and that is the use of the more inaccessible, but much more anatomically correct Cooper's ligament. The fact is that the inguinal ligament has fallen into serious disrepute as an anchoring structure.

In the repair of an indirect hernia no one would think of carefully suturing the internal oblique and transversus layers tightly about the cord at the abdominal inguinal ring without first isolating and doing a high ligation of the sac. It seems equally logical to me to treat the peritoneal diverticulum of a direct hernia, which is precisely the same structural defect except that it lies medial to the deep epigastric artery, in at least a similar manner. It is immaterial whether this peritoneal diverticulum presents in Hesselbach's triangle as a direct hernia, or along-

Presented during the annual assembly of The Southwestern Surgical Congress, Sept. 21–23, 1953, Salt Lake City, Utah.

side the femoral vein as a femoral hernia, it is still a hernia sac, and the fundamental defect which must be dealt with before it can be logically said that a sound anatomical attempt has been made at repair. For technical reasons, it is easier to convert a large direct sac to the indirect position before excision, but burying a sac of this variety under a mass of sutures most certainly invites recurrence.

The lower reaches of the aponeurosis of the transversus abdominis muscle and the underlying transversalis fascia medial to the deep epigastric artery are necessarily involved in direct or femoral hernia. The transversus aponeurosis inserts into the spine of the pubis and laterally along the iliopectineal line to the femoral vein. Here the transversus aponeurosis ends, but transversalis fascia expands and forms a sheath over the femoral vessels. This anatomic truth led to McVay's entirely logical suggestion that the transversus layers be sutured to the structure into which they properly insert, rather than displacing them 2 cm. in a superficial direction into a different anatomical plane. Once this much has been accomplished there are any number of acceptable methods of adding support to this space such as a flap from the rectus sheath, tantalum wire mesh, fascia lata, cutis grafts and others. The delightful truth seems to be however, that once the transversus layers are firmly sutured to Cooper's ligament, these adjuncts are usually not necessary.

It should be apparent that this method is equally effective for both direct and femoral hernias. In femoral hernia the insertion of the transversus aponeurosis is displaced medially by the sac of peritoneum which insinuates itself into and enlarges the hiatus between the transversus fibers and the vein. The transversus aponeurosis and the transversalis fascia are usually of good quality in femoral hernia and can be sutured securely to Cooper's ligament after ligation and excision of the peritoneal sac. It is unnecessary to suture the inguinal ligament to Cooper's ligament in this repair. In direct hernia as well as femoral hernia repair it is important to suture transversalis fascia to the femoral sheath over the top of the vessels far enough laterally to make a snug abdominal inguinal ring. It is patently obvious that care must be taken to avoid injury to the femoral vessels during this maneuver.

McVay excises an elipse of thinned out transversus layers from the femoral vessels down to Cooper's ligament. He then makes a relaxing incision in the aponeuroses of the internal oblique and transversus abdominis as they pass over the rectus muscle, leaving the aponeurosis of the external oblique intact. By this method the transversus layers may be sutured to Cooper's ligament without tension. This was suggested many years ago by Halsted. Halsted himself however, pointed out that it left a potential site for hernia alongside the rectus sheath. It is my own practice to separate the aponeurosis of the transversus abdominis muscle from the underlying transversalis fascia and suture the latter to Cooper's ligament with interrupted nonabsorbable sutures. Transversalis fascia comes down easily; makes a solid repair and obviates the necessity for making a relaxing incision. It is my personal belief that the conjoined tendon should be carefully held out of the way by an intern when doing a hernia repair.

A large indirect hernia may push the deep epigastric vessels over to the edge

of the rectus muscle. Here the defect presents the same anatomical problem as that seen in direct hernia, and after the sac is properly treated it may be effectively repaired in exactly the same manner which is used in the repair of direct hernia. In dealing with a small patent processus vaginalis in an infant or young person in whom there is no significant defect alongside the cord at the level of the abdominal inguinal ring, high ligation of the sac alone is necessary. Palpation of the direct and femoral spaces through the indirect opening should be done as a routine, and when these spaces are not defective it is not only unnecessary, but probably harmful to suture the conjoined tendon to the inguinal ligament.

I think if we will be absolutely honest, most of us have had the experience of doing what we considered to be an excellent repair of the floor of the inguinal canal only to have the patient come back in a few months with a recurrence at the level of the abdominal inguinal ring. A minute peritoneal diverticulum at the internal ring can be responsible for this distressing situation. For this reason I would like to stress that merely opening the cremaster layer in the midportion of the cord and blithely assuming that there is no indirect element to this hernia above is very wrong indeed. The internal oblique muscle must be retracted away from the level of the internal abdominal ring and the cremaster must be opened to its origin. In so doing, many a small diverticulum will be discovered and a recurrent hernia thereby prevented.

HOWARD T. ROBERTSON, M.D.
Assistant Clinical Professor of Surgery
University of Colorado School of Medicine

Denver, Colorado

BOOK REVIEWS

The editors of The American Surgeon will at all times welcome new books in the field of surgery and will acknowledge their receipt in these pages. The editors do not, however, agree to review all books that have been submitted without solicitation.

The Radiology of Bones and Joints. An Introduction to the Study of Tumours and other Diseases of Bone. By JAMES F. BRAILSFORD, M.D., Ph.D., F.R.C.P., F.I.C.S.(Hon.) Hunterian Professor, Royal College of Surgeons, England, 1934–5, 1943–4; Founder and first President of the British Association of Radiologists (now the Faculty of Radiologists); Emeritus Director of Radiological Studies in Living Anatomy, The University of Birmingham; Consulting Radiologist to the Queen Elizabeth Hospital, Birmingham, The Royal Orthopedic Hospital, The Accident Hospital and The Warwickshire Orthopedic Hospital, and other hospitals of the City; Active Fellow, British Orthopedic Association; Awarded The Robert Jones Gold Medal and Prize of The British Orthopedic Association, 1927, The Roentgen Prize, 1936, Encomienda Order Civil De Sanidad, Spanish Government, 1st Dallas B. Phemister Memorial Lectureship, University of Chicago, Hon. Socio Academia of Surgery, Madrid, Hon. Member University of Bordeaux, Hon. Member Roentgen Societies of Chicago, Detroit, New York and Texas. Fifth Edition. A volume of 875 pages with over 725 illustrations. Baltimore, Maryland, The Williams & Wilkins Company, 1953. Price $19.00.

This very interesting and well written treatise on pathology of bones and joints as revealed by the radiograph, is a summation of the author's vast experience since he was appointed to the staff of the Pathological department of the University of Birmingham, 46 years ago. In addition he has utilized the contribution of 157 recent publications on the subject of bone and joint disease. The author shows in his description of various pathologic processes that his judgment is tempered with experience. The book has many characteristic illustrations of the pathologic processes discussed. In addition the author has personally contributed many line drawings, which add to the interest and educational value of the book.

Part I is divided into a discussion of the various anatomic divisions of the skeleton, starting with the skeleton at birth and prior to birth. The discussion of each anatomic part is extremely comprehensive. For instance the chapter on the hand and wrist discusses normal ossification, normal sesamoids and variation from the normal. The manifestation of the various types of arthritis, gout, Charcot's joints, osteitis, sarcoid, achondroplasia and various congenital anomalies are among the many different entities described.

Part II is a discussion of the abnormalities and pathology of bones and joints. It is a general discussion. This consists of four chapters. Dysplasia of bone, generalized diseases of the skeleton, neurotrophic changes in joints, and bone tumors constitute the subject matter of these last four chapters.

The author has a style of writing that intrigues the casual reader. Interest is enhanced by many references to personal experience. The author's wide experience has made it possible for him to follow up cases in some instances for many years, a contribution not possible by a younger author.

We have the usual reversal of print of radiographs characteristic of books published by English authors. If one disregards this slight distraction the radiographs presented in most instances beautifully visualize the pathology discussed. What the radiographs may lack is made up by the line drawings.

This book is considered an excellent summary of the study of pathology of bones and joints. The division of subject matter into sections is sharply demarcated. It should be available to any Radiologist and Orthopedist as a means of quickly obtaining information about both common and unusual pathologic bone and joint conditions.

GALEN M. TICE, M.D.

Surgery of Repair as Applied to Hand Injuries. By RANK, B. K., M.S. (Melbourne), F.R.C.S. (England), F.R.A.C.S. Honorary Plastic Surgeon, Royal Melbourne Hospital; Visiting Plastic Surgeon, Repatriation Commission, Victoria; Consulting Plastic Surgeon, Ministry of Health in Tasmania and WAKEFIELD, A. R., M.S. (Melbourne), F.R.C.S. (England), F.R.A.C.S. Honorary Plastic Surgeon, Children's Hospital, Melbourne; Honorary Assistant Plastic Surgeon, Royal Melbourne Hospital; Visiting Plastic Surgeon, Repatriation Commission, Victoria. Foreword by SIR GORDON GORDON-TAYLOR, K.B.E., C.B., LL.D., Sc.D., F.R.C.S., F.R.C.S. (Ed), F.R.A.C.S., F.A.C.S., F.R.C.S., (Canada) E. & S. Livingstone, Ltd. Edinburgh and London, and The Williams & Wilkins Co., 1953. Price $8.00.

This timely book summarizes the basic principles of surgery as applied to hand injuries. The social significance of such injuries makes it mandatory for the surgeon to obtain the best possible result when the patient is first seen. Late secondary reparative surgery can then often be minimized and a better functional result will be gained. The authors point out the likelihood of multiple injuries, and the necessity that the attending surgeon be versed in the principles of orthopedics, peripheral nerve injury, tendon repair and primary coverage.

The indications for the treatment of fresh and contaminated hand wounds are well covered. Burns of the hand are dealt with in a special section. Emphasis is rightly placed upon the fundamental concept that primary healing of a hand wound will give the best functional results. The various necessary methods needed to provide an adequate skin coverage are presented.

This book is well organized and written with a delightful clarity.

CREIGHTON A. HARDIN, M.D.

A Practice of Thoracic Surgery. By A. L. D'ABREU, London, Edward Arnold & Co. American Distributors: Baltimore, Maryland, The Williams & Wilkins Co.

The purpose of this 591 page text on Thoracic Surgery as stated by the author is to present to physicians, general practitioners, and young surgeons *a method* of thoracic surgical practice including the fundamental ancillary subjects and technics. The text is divided by subject material into seven parts. Each part is concisely covered in an easily understandable fashion, written by the author and outstanding British authorities in each subject. There are numerous excellent illustrations. The section on carcinoma of the lung is especially well presented.

Ancillary basic physiology is well covered. The text is not intended as a detailed reference source for thoracic surgeons, but rather as a text for student and surgical resident use.

This volume is a valuable addition to medical literature within the limitations of the scope for which it was written.

ROBERT G. RATE, M.D.